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(71) Applicant: EOS BIOTECHNOLOGY, INC. [US/US]; 225A Gateway Boulevard, South San Francisco, CA 94080 (US).

(72) Inventors: AFAR, Daniel, E., H.; 435 Visitacion Avenue, Brisbane, CA 94005 (US). AGUS, David; 522 North Crescent Drive, Beverly Hills, CA 90210 (US). MACK, David, H.; 2076 Montercy Avenue, Menlo Park, CA 94025 (US). ning of each regular issue of the PCT Gazette.

(74) Agents: BASTIAN, Kevin, L. et al.; Townsend and Townsend and Crew LLP, Two Embarcadero Center, Eighth Floor, San Francisco, CA 94111 (US).

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(57) Abstract: Described herein are genes whose expression are up-regulated or down-regulated in prostate cancer. Also described are such genes whose expression is further up-regulated or down-regulated in drug-resistant prostate cancer cells. Related methods and compositions that can be used for diagnosis and treatment of prostate cancer are disclosed. Also described herein are methods that can be used to identify modulators of prostate cancer.

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METHODS OF DIAGNOSIS AND TREATMENT OF ANDROGEN-DEPENDENT PROSTATE CANCER, PROSTATE CANCER UNDERGOING ANDROGEN WITHDRAWAL, AND ANDROGEN-INDEPENDENT PROSTATE CANCER

CROSS-REFERENCES TO RELATED APPLICATIONS

This application claims priority from the following applications: USSN 60/295,917, filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed November 13, 2001; and USSN 60/372,246, filed April 12, 2002; each of which is incorporated herein by reference in its entirety.

FIELD OF THE INVENTION

The invention relates to the identification of nucleic acid and protein expression profiles and nucleic acids, products, and antibodies thereto that are involved in prostate cancer; and to the use of such expression profiles and compositions in the diagnosis, prognosis, and therapy of prostate cancer. The invention further relates to methods for identifying and using agents and/or targets that inhibit prostate cancer.

BACKGROUND OF THE INVENTION

Prostate cancer is the most frequently diagnosed cancer and the second leading cause of male cancer death in North America and northern Europe. Early detection of prostate cancer using a serum test for prostate-specific antigen (PSA) has dramatically improved the treatment of the disease (Oesterling (1992) J. Am. Med. Assoc., 267:2236-2238). Treatment of prostate cancer consists largely of surgical prostatectomy, radiation therapy, androgen ablation therapy and chemotherapy. Although many prostate cancer patients are effectively treated, the current therapies can all induce serious side effects which diminish quality of life. Patients who present with metastatic disease are most often treated with androgen-ablation therapy. Hormone blockade results in significant regression of the tumor. However, this treatment rarely cures the patient and invariably results in progression to androgen-

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independent disease, which is incurable. Afrin and Stuart (1994) <u>J.S.C. Med. Assoc.</u> 90:231-236.

The identification of novel therapeutic targets and diagnostic markers is essential for improving the current treatment of prostate cancer patients. Recent advances in molecular medicine have increased the interest in tumor-specific cell surface antigens that could serve as targets for various immunotherapeutic or small molecule strategies. Antigens suitable for immunotherapeutic strategies should be highly expressed in cancer tissues and ideally not expressed in normal adult tissues. Expression in tissues that are dispensable for life, however, may be tolerated. Examples of such antigens include Her2/neu and the B-cell antigen CD20. Humanized monoclonal antibodies directed to Her2/neu (Herceptin) are currently in use for the treatment of metastatic breast cancer. Ross and Fletcher (1998) Stem Cells 16:413-428. Similarly, anti-CD20 monoclonal antibodies (Rituxin) are used to effectively treat non-Hodgkin's lymphoma. Maloney, et al. (1997) Blood 90:2188-2195; Leget and Czuczman (1998) Curr. Opin. Oncol. 10:548-551.

Several potential immunotherapeutic targets have been identified for prostate cancer. They include prostate-specific membrane antigen (PSMA) (Israeli, et al. (1993) Cancer Res. 53:227-230), prostate stem cell antigen (PSCA; Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740), and serpentine transmembrane epithelial antigen of the prostate (STEAP: Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). PSMA is a type II transmembrane hydrolase with significant homology to a rat neuropeptidase (Carter, et al. (1996) Proc. Natl. Acad. Sci. USA 93:749-753). Antibodies directed towards PSMA are currently being used to detect metastasized prostate cancer as the Prostascint Scan (Sodee, et al. (1996) Clin, Nucl. Med. 21:759-767) and are also being evaluated for treatment of advanced disease (Gregorakis, et al. (1998) Semin, Urol, Oncol, 16:2-12; Liu, et al. (1998) Cancer Res. 58:4055-4060; Murphy, et al. (1998) J. Urol. 160:2396-2401). In a study on bone metastasis of prostate cancer, only 8 out of 18 patient samples expressed PSMA (Silver, et al. (1997) Clin. Cancer Res. 3:81-85). Therefore, it is clear that other targets need to be identified to manage metastasized disease. PSCA is a member of the Thy-1/Ly-6 family of glycosylphosphatidylinositol-linked plasma membrane proteins (Reiter, et al. (1998) Proc. Natl. Acad. Sci. USA 95:1735-1740). Immunohistochemical data shows that PSCA is upregulated in the majority of prostate cancer epithelia and is also detected in bone metastasis (Gu, et al. (2000) Oncogene 19:1288-1296). Recent work shows that antibodies directed to

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PSCA can prevent metastatic spread of prostate cancer in a mouse model (Saffran, et al. (2001) Proc. Natl. Acad. Sci. USA 98:2658-2663). STEAP is a multi-transmembrane prostate-specific protein that may function as a channel or transporter protein (Hubert, et al. (1999) Proc. Natl. Acad. Sci. USA 96:14529-14534). Its protein expression is specific to the basolateral membranes of normal prostate and prostate cancer epithelia. STEAP expression was most highly concentrated at cell-cell boundaries, implying a potential function in intercellular communication. Therapeutic monoclonal antibodies have so far not been reported for STEAP.

SUMMARY OF THE INVENTION

The present invention therefore provides nucleotide sequences of genes that are upand down-regulated in androgen-independent prostate cancer cells or prostate cells
undergoing androgen withdrawal. Such genes are useful for diagnostic purposes, and also as
targets for screening for therapeutic compounds that modulate prostate cancer, such as
hormones or antibodies. Other aspects of the invention will become apparent to the skilled
artisan by the following description of the invention.

In one aspect, the present invention provides a method of detecting an androgen independent prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to nucleic acid molecule comprising a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In one embodiment, the present invention provides a method of determining the level of a prostate cancer associated transcript in a cell from a patient.

In one embodiment, the present invention provides a method of detecting a prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4.

In various embodiments, the polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4; the polynucleotide comprises a sequence as shown in Tables 1A-4; the biological sample is a tissue sample; the biological sample comprises isolated nucleic acids, e.g., mRNA; the polynucleotide is labeled, e.g., with a fluorescent label; the polynucleotide is immobilized on a solid surface; the patient is

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undergoing a therapeutic regimen to treat prostate cancer; the patient is suspected of having metastatic prostate cancer; the patient is a human; the patient is suspected of having a taxol-resistant cancer: or the prostate cancer associated transcript is mRNA.

In other embodiments, the method further comprises the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.

• In another aspect, the present invention provides a method of monitoring the efficacy of a therapeutic treatment of prostate cancer, the method comprising the steps of: (i) providing a biological sample from a patient undergoing the therapeutic treatment; and (ii) determining the level of a prostate cancer-associated transcript in the biological sample by contacting the biological sample with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4, thereby monitoring the efficacy of the therapy. In a further embodiment, the patient has metastatic prostate cancer. In a further embodiment, the patient has a drug resistant (e.g., taxol resistant) form of prostate cancer.

In one embodiment, the method further comprises the step of: (iii) comparing the level of the prostate cancer-associated transcript to a level of the prostate cancer-associated transcript in a biological sample from the patient prior to, or earlier in, the therapeutic treatment.

Additionally, provided herein is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a patient and removing a cell sample from the patient. The expression profile of the cell is then determined. This method may further comprise comparing the expression profile to an expression profile of a healthy individual. In a preferred embodiment, said expression profile includes a gene of Tables 1A-4.

In one aspect, the present invention provides an isolated nucleic acid molecule consisting of a polynucleotide sequence as shown in Tables 1A-4.

In one embodiment, an expression vector or cell comprises the isolated nucleic acid.

In one aspect, the present invention provides an isolated polypeptide which is encoded by a nucleic acid molecule having polypucleotide sequence as shown in Tables 1A-4.

In another aspect, the present invention provides an antibody that specifically binds to an isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

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In certain embodiments, the antibody is conjugated to an effector component, e.g., a fluorescent label, a radioisotope or a cytotoxic chemical; the antibody is an antibody fragment; or the antibody is humanized.

In one aspect, the present invention provides a method of detecting a prostate cancer cell in a biological sample from a patient, the method comprising contacting the biological sample with an antibody as described herein.

In another aspect, the present invention provides a method of detecting antibodies specific to prostate cancer in a patient, the method comprising contacting a biological sample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from Tables 1A-4.

In another aspect, the present invention provides a method for identifying a compound that modulates a prostate cancer-associated polypeptide, the method comprising the steps of:
a) contacting the compound with a prostate cancer-associated polypeptide, the polypeptide encoded by a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4; and b) determining the functional effect of the compound upon the polypeptide.

In one embodiment, the functional effect is a physical effect, an enzymatic effect, or a chemical effect.

In one embodiment, the polypeptide is expressed in a eukaryotic host cell or cell membrane. In another embodiment, the polypeptide is recombinant.

In one embodiment, the functional effect is determined by measuring ligand binding to the polypeptide.

In another aspect, the present invention provides a method of inhibiting proliferation of a prostate cancer-associated cell to treat prostate cancer in a patient, the method comprising the step of administering to the subject a therapeutically effective amount of a compound identified as described herein.

In one embodiment, the compound is an antibody.

In another aspect, the present invention provides a drug screening assay comprising the steps of: a) administering a test compound to a mammal having prostate cancer or to a cell sample isolated therefrom; b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the

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polynucleotide in a control cell sample or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the treatment of prostate cancer.

In one embodiment, the control is a mammal with prostate cancer or a cell sample therefrom that has not been treated with the test compound. In another embodiment, the control is a normal cell or mammal.

In one embodiment, the test compound is administered in varying amounts or concentrations. In another embodiment, the test compound is administered for varying time periods. In another embodiment, the comparison can occur after addition or removal of the drug candidate.

In one embodiment, the levels of a plurality of polynucleotides that selectively hybridize to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 are individually compared to their respective levels in a control cell sample or mammal. In a preferred embodiment the plurality of polynucleotides is from three to ten.

15 In another aspect, the present invention provides a method for treating a mammal having prostate cancer comprising administering a compound identified by the assay described herein.

In another aspect, the present invention provides a pharmaceutical composition for treating a mammal having prostate cancer, the composition comprising a compound identified by the assay described herein and a physiologically acceptable excipient.

In one aspect, the present invention provides a method of screening drug candidates by providing a cell expressing a gene that is up- and down-regulated as in a prostate cancer. In one embodiment, a gene is selected from Tables 1A-4. The method further includes adding a drug candidate to the cell and determining the effect of the drug candidate on the expression of the expression profile gene.

In one embodiment, the method of screening drug candidates includes comparing the level of expression in the absence of the drug candidate to the level of expression in the presence of the drug candidate, wherein the concentration of the drug candidate can vary when present, and wherein the comparison can occur after addition or removal of the drug candidate. In a preferred embodiment, the cell expresses at least two expression profile genes. The profile genes may show an increase or decrease.

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Also provided is a method of evaluating the effect of a candidate prostate cancer drug comprising administering the drug to a transgenic animal expressing or over-expressing the prostate cancer modulatory protein, or an animal lacking the prostate cancer modulatory protein, for example as a result of a gene knockout.

Moreover, provided herein is a biochip comprising one or more nucleic acid segments of Tables 1A-4, wherein the biochip comprises fewer than 1000 nucleic acid probes.

Preferably, at least two nucleic acid segments are included. More preferably, at least three nucleic acid segments are included.

Furthermore, a method of diagnosing a disorder associated with prostate cancer is provided. The method comprises determining the expression of a gene of Tables 1A-4, in a first tissue type of a first individual, and comparing the distribution to the expression of the gene from a second normal tissue type from the first individual or a second unaffected individual. A difference in the expression indicates that the first individual has a disorder associated with prostate cancer.

15 In a further embodiment, the biochip also includes a polynucleotide sequence of a gene that is not up- and down-regulated in prostate cancer.

In one embodiment a method for screening for a bioactive agent capable of interfering with the binding of a prostate cancer modulating protein (prostate cancer modulatory protein) or a fragment thereof and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. In a preferred embodiment, the method comprises combining a prostate cancer modulatory protein or fragment thereof, a candidate bioactive agent and an antibody which binds to said prostate cancer modulatory protein or fragment thereof. The method further includes determining the binding of said prostate cancer modulatory protein or fragment thereof and said antibody. Wherein there is a change in binding, an agent is identified as an interfering agent. The interfering agent can be an agonist or an antagonist. Preferably, the agent inhibits prostate cancer.

Also provided herein are methods of eliciting an immune response in an individual. In one embodiment a method provided herein comprises administering to an individual a composition comprising a prostate cancer modulating protein, or a fragment thereof. In another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4.

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Further provided herein are compositions capable of eliciting an immune response in an individual. In one embodiment, a composition provided herein comprises a prostate cancer modulating protein, preferably encoded by a nucleic acid of Tables 1A-4, or a fragment thereof, and a pharmaceutically acceptable carrier. In another embodiment, said composition comprises a nucleic acid comprising a sequence encoding a prostate cancer modulating protein, preferably selected from the nucleic acids of Tables 1A-4 and a pharmaceutically acceptable carrier.

Also provided are methods of neutralizing the effect of a prostate cancer protein, or a fragment thereof, comprising contacting an agent specific for said protein with said protein in an amount sufficient to effect neutralization. In another embodiment, the protein is encoded by a nucleic acid selected from those of Tables 1A-4. In another aspect of the invention, a method of treating an individual for prostate cancer is provided. In one embodiment, the method comprises administering to said individual an inhibitor of a prostate cancer modulating protein. In another embodiment, the method comprises administering to a patient having prostate cancer an antibody to a prostate cancer modulating protein conjugated to a therapeutic moiety. Such a therapeutic moiety can be a cytotoxic agent or a radioisotope.

DETAILED DESCRIPTION OF THE INVENTION

In accordance with the objects outlined above, the present invention provides novel methods for diagnosis and evaluation of androgen-dependent prostate cells (malignant or non-malignant), prostate cells undergoing androgen withdrawal, and androgen-independent prostate cancer, as well as methods for treating androgen-dependent prostate cells (malignant or non-malignant), prostate cancer undergoing androgen withdrawal, and androgen-independent prostate cancer. The current Specification incorporates the text of USSN 09/976,858, filed October 12, 2001, USSN 60/295,917, filed June 4, 2001, USSN 60/368,689, filed March 29, 2002; USSN 60/350,666, filed November 13, 2001; and USSN 60/372,246, filed April 12, 2002.

Table 1A provides unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-independent prostate cancer samples. Table 1A also provides an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Table 1A can be broadly defined into the following categories:

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Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in table 1A). Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in 1A). Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in table 1A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-hi pattern in table 1A).

Tables 2A-C provide unigene cluster identification numbers for the nucleotide sequence of genes that exhibit increased or decreased expression in androgen-dependent prostate cancer, prostate cancer undergoing androgen withdrawal and androgen-independent prostate cancer. Tables 2A-C also provide an exemplar accession number that provides a nucleotide sequence that is part of the unigene cluster. The expression patterns of the genes of Tables 2A-C can be broadly defined into the following 6 categories:

Genes that are expressed early in the time course of androgen withdrawal, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A). Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgen-independence (hi-lo-lo-lo pattern in Table 2A). Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of androgen-independence (hi-hi-lo-lo pattern in Table 2A). Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-lo-hi-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

Definitions

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The term "androgen ablation therapy" refers to techniques for the removal or destruction of sources of male hormones, such as testosterone. These techniques include, for example, 1) surgical removal of the testicles, 2) medications such as gonadatropin releasing hormone analogs that inhibit testosterone production, or 3) anti-androgenic drugs that block androgen receptors.

The term "androgen-independent prostate cancer protein" or "androgen-independent prostate cancer polynucleotide" or "androgen-independent prostate cancer-associated transcript" refers to nucleic acid and polypeptide polymorphic variants, alleles, mutants, and interspecies homologues that: (1) have a nucleotide sequence that has greater than about 60% nucleotide sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater nucleotide sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more nucleotides, to a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4; (2) bind to antibodies, e.g., polyclonal antibodies, raised against an immunogen comprising an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4 and conservatively modified variants thereof; (3) specifically hybridize under stringent hybridization conditions to a nucleic acid sequence, or the complement thereof of Tables 1A-4 and conservatively modified variants thereof; or (4) have an amino acid sequence that has greater than about 60% amino acid sequence identity, 65%, 70%, 75%, 80%, 85%, 90%, preferably 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98% or 99% or greater amino sequence identity, preferably over a region of over a region of at least about 25, 50, 100, 200, 500, 1000, or more amino acid, to an amino acid sequence encoded by a nucleotide sequence of or associated with a unigene cluster of Tables 1A-4. These polynucleotides or proteins may also be expressed during a period following androgen withdrawal. A polynucleotide or polypeptide sequence is typically from a mammal including, but not limited to, primate, e.g., human; rodent, e.g., rat, mouse, hamster; cow, pig, horse, sheep, or other mammal. A "prostate cancer polypeptide" and a "prostate cancer polynucleotide," include both naturally occurring or recombinant forms, and may refer to those polypeptides or polynucleotides which are expressed in prostate proliferative cells.

A "full length" prostate cancer protein or nucleic acid refers to a prostate cancer polypeptide or polynucleotide sequence, or a variant thereof, that contains the elements normally contained in one or more naturally occurring, wild type prostate cancer

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polynucleotide or polypeptide sequences. The "full length" may be prior to, or after, various stages of post-translation processing or splicing, including alternative splicing.

"Biological sample" as used herein is a sample of biological tissue or fluid that contains nucleic acids or polypeptides, e.g., of a prostate cancer protein, polynucleotide or transcript. Such samples include, but are not limited to, tissue isolated from primates, e.g., humans, or rodents, e.g., mice, and rats. Biological samples may also include sections of tissues such as biopsy and autopsy samples, frozen sections taken for histology purposes, blood, plasma, serum, sputum, stool, tears, mucus, hair, skin, etc. Biological samples also include explants and primary and/or transformed cell cultures derived from patient tissues. A biological sample is typically obtained from a cukaryotic organism, most preferably a mammal such as a primate e.g., chimpanzee or human; cow; dog; cat; a rodent, e.g., guinea pig, rat, mouse; rabbit; or a bird; reptile; or fish.

"Providing a biological sample" means to obtain a biological sample for use in methods described in this invention. Most often, this will be done by removing a sample of cells from an animal, but can also be accomplished by using previously isolated cells (e.g., isolated by another person, at another time, and/or for another purpose), by collecting a sample which contains a soluble polypeptide or nucleic acid derived from a prostate cell, or by performing the methods of the invention in vivo. Archival tissues, having treatment or outcome history, will be particularly useful.

The terms "identical" or percent "identity," in the context of two or more nucleic acids or polypeptide sequences, refer to two or more sequences or subsequences that are the same or have a specified percentage of amino acid residues or nucleotides that are the same (i.e., about 60% identity, preferably 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or higher identity over a specified region, when compared and aligned for maximum correspondence over a comparison window or designated region) as measured using a BLAST or BLAST 2.0 sequence comparison algorithms with default parameters described below, or by manual alignment and visual inspection (see, e.g., NCBI web site http://www.ncbi.nlm.nih.gov/BLAST/ or the like). Such sequences are then said to be "substantially identical." This definition also refers to, or may be applied to, the compliment of a test sequence. The definition also includes sequences that have deletions and/or additions, as well as those that have substitutions, as well as naturally occurring, e.g., polymorphic or allelic variants, and man-made variants. As described below, the preferred

algorithms can account for gaps and the like. Preferably, identity exists over a region that is at least about 25 amino acids or nucleotides in length, or more preferably over a region that is 50-100 amino acids or nucleotides in length.

For sequence comparison, typically one sequence acts as a reference sequence, to which test sequences are compared. When using a sequence comparison algorithm, test and reference sequences are entered into a computer, subsequence coordinates are designated, if necessary, and sequence algorithm program parameters are designated. Preferably, default program parameters can be used, or alternative parameters can be designated. The sequence comparison algorithm then calculates the percent sequence identities for the test sequences relative to the reference sequence, based on the program parameters.

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A "comparison window", as used herein, includes reference to a segment of one of the number of contiguous positions selected from the group consisting typically of from 20 to 600, usually about 50 to about 200, more usually about 100 to about 150 in which a sequence may be compared to a reference sequence of the same number of contiguous positions after the two sequences are optimally aligned. Methods of alignment of sequences for comparison are well-known in the art. Optimal alignment of sequences for comparison can be conducted, e.g., by the local homology algorithm of Smith and Waterman (1981) Appl. Math. 2:482, by the homology alignment algorithm of Needleman and Wunsch (1970) J. Mol. Biol. 48:443-453, by the search for similarity method of Pearson and Lipman (1988) Proc. Nat'l. Acad. Sci. USA 85:2444-2448, by computerized implementations of these algorithms (GAP, BESTFIT, FASTA, and TFASTA in the Wisconsin Genetics Software Package, Genetics Computer Group, 575 Science Dr., Madison, WI), or by manual alignment and visual inspection (see, e.g., Ausubel, et al. (eds. 1995 and supplements) Current Protocols in Molecular Biology Limincott).

Preferred examples of algorithms that are suitable for determining percent sequence identity and sequence similarity include the BLAST and BLAST 2.0 algorithms, which are described in Altschul, et al. (1977) Nuc. Acids Res. 25:3389-3402 and Altschul, et al. (1990) J. Mol. Biol. 215:403-410. BLAST and BLAST 2.0 are used, with the parameters described herein, to determine percent sequence identity for the nucleic acids and proteins of the invention. Software for performing BLAST analyses is publicly available through the National Center for Biotechnology Information (http://www.ncbi.nlm.nih.gov/). This algorithm involves first identifying high scoring sequence pairs (HSPs) by identifying short

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words of length W in the query sequence, which either match or satisfy some positive-valued threshold score T when aligned with a word of the same length in a database sequence. T is referred to as the neighborhood word score threshold (Altschul, et al., supra). These initial neighborhood word hits act as seeds for initiating searches to find longer HSPs containing them. The word hits are extended in both directions along each sequence for as far as the cumulative alignment score can be increased. Cumulative scores are calculated using, e.g., for nucleotide sequences, the parameters M (reward score for a pair of matching residues; always > 0) and N (penalty score for mismatching residues; always < 0). For amino acid sequences, a scoring matrix is used to calculate the cumulative score. Extension of the word hits in each direction are halted when: the cumulative alignment score falls off by the quantity X from its maximum achieved value; the cumulative score goes to zero or below, due to the accumulation of one or more negative-scoring residue alignments; or the end of either sequence is reached. The BLAST algorithm parameters W. T. and X determine the sensitivity and speed of the alignment. The BLASTN program (for nucleotide sequences) uses as defaults a wordlength (W) of 11, an expectation (E) of 10, M=5, N=-4 and a comparison of both strands. For amino acid sequences, the BLASTP program uses as defaults a wordlength of 3, and expectation (E) of 10, and the BLOSUM62 scoring matrix (see Henikoff and Henikoff (1989) Proc. Natl. Acad. Sci. USA 89:10915-919) alignments (B) of 50, expectation (E) of 10, M=5, N=-4, and a comparison of both strands.

The BLAST algorithm also performs a statistical analysis of the similarity between two sequences (see, e.g., Karlin and Altschul (1993) Proc. Nat'l. Acad. Sci. USA 90:5873-5787). One measure of similarity provided by the BLAST algorithm is the smallest sum probability (P(N)), which provides an indication of the probability by which a match between two nucleotide or amino acid sequences would occur by chance. For example, a nucleic acid is considered similar to a reference sequence if the smallest sum probability in a comparison of the test nucleic acid to the reference nucleic acid is less than about 0.2, more preferably less than about 0.01, and most preferably less than about 0.001. Log values may be large negative numbers, e.g., 5, 10, 20, 30, 40, 40, 70, 90, 110, 150, 170, etc.

An indication that two nucleic acid sequences or polypeptides are substantially identical is that the polypeptide encoded by the first nucleic acid is immunologically cross reactive with the antibodies raised against the polypeptide encoded by the second nucleic acid, as described below. Thus, a polypeptide is typically substantially identical to a second

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polypeptide, e.g., where the two peptides differ only by conservative substitutions. Another indication that two nucleic acid sequences are substantially identical is that the two molecules or their complements hybridize to each other under stringent conditions, as described below. Yet another indication that two nucleic acid sequences are substantially identical is that the same primers can be used to amplify the sequences.

A "host cell" is a naturally occurring cell or a transformed cell that contains an expression vector and supports the replication or expression of the expression vector. Host cells may be cultured cells, explants, cells in vivo, and the like. Host cells may be prokaryotic cells such as E. coli, or eukaryotic cells such as yeast, insect, amphibian, or mammalian cells such as CHO, HeLa, and the like (see, e.g., the American Type Culture Collection catalog or web site, www.atcc.org).

The terms "isolated," "purified," or "biologically pure" refer to material that is substantially or essentially free from components that normally accompany it as found in its native state. Purity and homogeneity are typically determined using analytical chemistry techniques such as polyacrylamide gel electrophoresis or high performance liquid chromatography. A protein or nucleic acid that is the predominant species present in a preparation is substantially purified. In particular, an isolated nucleic acid is separated from some open reading frames that naturally flank the gene and encode proteins other than protein encoded by the gene. The term "purified" in some embodiments denotes that a nucleic acid or protein gives rise to essentially one band in an electrophoretic gel. Preferably, it means that the nucleic acid or protein is at least 85% pure, more preferably at least 95% pure, and most preferably at least 99% pure. "Purify" or "purification" in other embodiments means removing at least one contaminant from the composition to be purified. In this sense, purification does not require that the purified compound be homogenous, e.g., 100% pure.

The terms "polypeptide," "peptide," and "protein" are used interchangeably herein to refer to a polymer of amino acid residues. The terms apply to amino acid polymers in which one or more amino acid residue is an artificial chemical mimetic of a corresponding naturally occurring amino acid, as well as to naturally occurring amino acid polymers, those containing modified residues, and non-naturally occurring amino acid polymer. Certain diagnostic methods may evaluate secreted or breakdown products present only because the producing cell is present, and would otherwise be absent in a normal individual.

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The term "amino acid" refers to naturally occurring and synthetic amino acids, as well as amino acid analogs and amino acid mimetics that function similarly to the naturally occurring amino acids. Naturally occurring amino acids are those encoded by the genetic code, as well as those amino acids that are later modified, e.g., hydroxyproline, γ -carboxyglutamate, and O-phosphoserine. Amino acid analogs refers to compounds that have the same basic chemical structure as a naturally occurring amino acid, e.g., an α carbon that is bound to a hydrogen, a carboxyl group, an amino group, and an R group, e.g., homoserine, norleucine, methionine sulfoxide, methionine methyl sulfonium. Such analogs may have modified R groups (e.g., norleucine) or modified peptide backbones, but retain the same basic chemical structure as a naturally occurring amino acid. Amino acid mimetics refers to chemical compounds that have a structure that is different from the general chemical structure of an amino acid, but that functions similarly to a naturally occurring amino acid.

Amino acids may be referred to herein by either their commonly known three letter symbols or by the one-letter symbols recommended by the IUPAC-IUB Biochemical Nomenclature Commission. Nucleotides, likewise, may be referred to by their commonly accepted single-letter codes.

"Conservatively modified variants" applies to both amino acid and nucleic acid sequences. With respect to particular nucleic acid sequences, conservatively modified variants refers to those nucleic acids which encode identical or essentially identical amino acid sequences, or where the nucleic acid does not encode an amino acid sequence, to essentially identical or associated, e.g., naturally contiguous, sequences. Because of the degeneracy of the genetic code, a large number of functionally identical nucleic acids encode most proteins. For instance, the codons GCA, GCC, GCG, and GCU encode the amino acid alanine. Thus, at every position where an alanine is specified by a codon, the codon can be altered to another of the corresponding codons described without altering the encoded polypeptide. Such nucleic acid variations are "silent variations," which are one species of conservatively modified variations. Every nucleic acid sequence herein which encodes a polypeptide also describes silent variations of the nucleic acid. One of skill will recognize that in certain contexts each codon in a nucleic acid (except AUG, which is ordinarily the only codon for methionine, and TGG, which is ordinarily the only codon for tryptophan) can be modified to yield a functionally identical molecule. Accordingly, often silent variations of

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a nucleic acid which encodes a polypeptide is implicit in a described sequence with respect to the expression product, but not with respect to actual probe sequences.

As to amino acid sequences, one of skill will recognize that individual substitutions, deletions or additions to a nucleic acid, peptide, polypeptide, or protein sequence which alters, adds or deletes a single amino acid or a small percentage of amino acids in the encoded sequence is a "conservatively modified variant" where the alteration results in the substitution of an amino acid with a chemically similar amino acid. Conservative substitutions providing functionally similar amino acids are well known in the art. Such conservatively modified variants are in addition to and do not exclude polymorphic variants, interspecies homologs, and alleles of the invention, typically conservative substitutions for one another: 1) Alanine (A), Glycine (G); 2) Aspartic acid (D), Glutamic acid (E); 3) Asparagine (N), Glutamine (Q); 4) Arginine (R), Lysine (K); 5) Isoleucine (I), Leucine (L), Methionine (M), Valine (V); 6) Phenylalanine (F), Tyrosine (Y), Tryptophan (W); 7) Serine (S), Threonine (T); and 8) Cysteine (C), Methionine (M) (see, e.g., Creighton (1984) Proteins Freeman).

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Macromolecular structures such as polypeptide structures can be described in terms of various levels of organization. For a general discussion of this organization, see, e.g., Alberts, et al. (2001) Molecular Biology of the Cell (4th ed.) and Cantor and Schimmel (1980) Biophysical Chemistry Part I: The Conformation of Biological Macromolecules Freeman. "Primary structure" refers to the amino acid sequence of a particular peptide. "Secondary structure" refers to locally ordered, three dimensional structures within a polypeptide. These structures are commonly known as domains. Domains are portions of a polypeptide that often form a compact unit of the polypeptide and are typically 25 to approximately 500 amino acids long. Typical domains are made up of sections of lesser organization such as stretches of β -sheet and α -helices. "Tertiary structure" refers to the complete three dimensional structure of a polypeptide monomer. "Quaternary structure" refers to the three dimensional structure formed, usually by the noncovalent association of independent tertiary units. Anisotropic terms are also known as energy terms.

"Nucleic acid" or "oligonucleotide" or "polynucleotide" or grammatical equivalents used herein means at least two nucleotides covalently linked together. Oligonucleotides are typically from about 5, 6, 7, 8, 9, 10, 12, 15, 25, 30, 40, 50 or more nucleotides in length, up to about 100 nucleotides in length. Nucleic acids and polynucleotides are a polymers of virtually any length, including longer lengths, e.g., 200, 300, 500, 1000, 2000, 3000, 5000,

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7000, 10,000, etc. A nucleic acid of the present invention will generally contain phosphodiester bonds, although in some cases, nucleic acid analogs are included that may have alternate backbones, comprising, e.g., phosphoramidate, phosphorothioate, phosphorodithioate, or O-methylphosphoroamidite linkages (see Eckstein (1992) Oligonucleotides and Analogues: A Practical Approach, Oxford University Press); and peptide nucleic acid backbones and linkages. Other analog nucleic acids include those with positive backbones; non-ionic backbones, and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7, ASC Symposium Series 580, Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids. Modifications of the ribose-phosphate backbone may be done for a variety of reasons, e.g., to increase the stability and half-life of such molecules in physiological environments or as probes on a biochip. Mixtures of naturally occurring nucleic acids and analogs can be made; alternatively, mixtures of different nucleic acid analogs, and mixtures of naturally occurring nucleic acids and analogs may be made.

A variety of references disclose such nucleic acid analogs, including, for example, phosphoramidate (Beaucage, et al. (1993) Tetrahedron 49(10):1925-1963 and references therein; Letsinger (1970) J. Org, Chem. 35:3800-3803; Sprinzl, et al. (1977) Eur. J. Biochem. 81:579-589; Letsinger, et al. (1986) Nucl. Acids Res. 14:3487-499; Sawai, et al (1984) Chem. Lett. 805, Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470-4471; and Pauwels, et al. (1986) Chemica Scripta 26:141-149), phosphorothioate (Mag, et al. (1991) Nucleic Acids Res. 19:1437-441; and U.S. Patent No. 5,644,048), phosphorodithioate (Briu, et al. (1989) J. Am. Chem. Soc. 111:2321-xxx, O-methylphosphoroamidite linkages (see Eckstein (1992) Oligonucleotides and Analogues: A Practical Approach Oxford University Press), and pentide nucleic acid backbones and linkages (see Egholm (1992) J. Am. Chem. Soc. 114:1895-1897; Meier, et al. (1992) Chem. Int. Ed. Engl. 31:1008-1010; Nielsen (1993) Nature 365:566-568; Carlsson, et al. (1996) Nature 380:207, each of which is incorporated by reference). Other analog nucleic acids include those with positive backbones (Denpcy, et al. (1995) Proc. Natl. Acad. Sci. USA 92:6097-101; non-ionic backbones (U.S. Patent Nos. 5,386,023, 5,637,684, 5,602,240, 5,216,141 and 4,469,863; Kiedrowshi, et al. (1991) Angew. Chem. Intl. Ed. English 30:423-426; Letsinger, et al. (1988) J. Am. Chem. Soc. 110:4470;

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Letsinger, et al. (1994) Nucleoside and Nucleotide 13:1597-xxx; Chapters 2 and 3 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580; Mesmaeker, et al. (1994) Bioorganic and Medicinal Chem. Lett. 4:395-xxx; Jeffs, et al. (1994) J. Biomolecular NMR 34:17; Hom (1996) Tetrahedron Lett. 37:743-xxx) and non-ribose backbones, including those described in U.S. Patent Nos. 5,235,033 and 5,034,506, and Chapters 6 and 7 in Sanghvi and Cook (eds. 1994) Carbohydrate Modifications in Antisense Research ACS Symposium Series 580. Nucleic acids containing one or more carbocyclic sugars are also included within one definition of nucleic acids (see Jenkins, et al. (1995) Chem. Soc. Rev. xx:169-176). Several nucleic acid analogs are described in Rawls (p. 35, June 2, 1997) C&E News. Each of these references is hereby expressly incorporated by reference.

Particularly preferred are peptide nucleic acids (PNA) which includes peptide nucleic acid analogs. These backbones are substantially non-ionic under neutral conditions, in contrast to the highly charged phosphodiester backbone of naturally occurring nucleic acids. This results in two advantages. First, the PNA backbone exhibits improved hybridization kinetics. PNAs have larger changes in the melting temperature ($T_{\rm m}$) for mismatched versus perfectly matched base pairs. DNA and RNA typically exhibit a 2-4° C drop in $T_{\rm m}$ for an internal mismatch. With the non-ionic PNA backbone, the drop is closer to 7-9° C. Similarly, due to their non-ionic nature, hybridization of the bases attached to these backbones is relatively insensitive to salt concentration. In addition, PNAs are not degraded by cellular enzymes, and thus can be more stable.

The nucleic acids may be single stranded or double stranded, as specified, or contain portions of both double stranded or single stranded sequence. As will be appreciated by those in the art, the depiction of a single strand also defines the sequence of the complementary strand; thus the sequences described herein also provide the complement of the sequence. The nucleic acid may be DNA, both genomic and cDNA, RNA or a hybrid, where the nucleic acid may contain combinations of deoxyribo- and ribo-nucleotides, and combinations of bases, including uracil, adenine, thymine, cytosine, guanine, inosine, xanthine hypoxanthine, isocytosine, isoguanine, etc. "Transcript" typically refers to a naturally occurring RNA, e.g., a pre-mRNA, hnRNA, or mRNA. As used herein, the term "nucleoside" includes nucleotides and nucleotide analogs, and modified nucleosides such as amino modified nucleosides. In addition, "nucleoside" includes non-naturally occurring analog structures.

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Thus, e.g., the individual units of a peptide nucleic acid, each containing a base, are referred to herein as a nucleoside.

A "label" or a "detectable moiety" is a composition detectable by spectroscopic, photochemical, biochemical, immunochemical, chemical, or other physical means. For example, useful labels include ³²P, fluorescent dyes, electron-dense reagents, enzymes (e.g., as commonly used in an ELISA), biotin, digoxigenin, or haptens and proteins or other entities which can be made detectable, e.g., by incorporating a radiolabel into the peptide or used to detect antibodies specifically reactive with the peptide. The labels may be incorporated into the prostate cancer nucleic acids, proteins, and antibodies at virtually any position. Many methods for conjugating the antibody to the label may be employed, including those methods described by Hunter, et al. (1962) Nature, 144:945; David, et al. (1974) Biochemistry 13:1014-1021; Pain, et al. (1981) J. Immunol. Meth. 40:219-230; and Nygren (1982) J. Histochem. and Cytochem. 30:407-412.

An "effector" or "effector moiety" or "effector component" is a molecule that is bound (or linked, or conjugated), either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds, to an antibody. The "effector" can be a variety of molecules including, e.g., detection moieties including radioactive compounds, fluorescent compounds, an enzyme or substrate, tags such as epitope tags, a toxin; activatable moieties, a chemotherapeutic agent; a lipase; an antibiotic; or a radioisotope emitting "hard" e.g., beta radiation.

A "labeled nucleic acid probe or oligonucleotide" is one that is bound, either covalently, through a linker or a chemical bond, or noncovalently, through ionic, van der Waals, electrostatic, or hydrogen bonds to a label such that the presence of the probe may be detected by detecting the presence of the label bound to the probe. Alternatively, method using high affinity interactions may achieve the same results where one of a pair of binding partners binds to the other, e.g., biotin, streptavidin.

As used herein a "nucleic acid probe or oligonucleotide" is defined as a nucleic acid capable of binding to a target nucleic acid of complementary sequence through one or more types of chemical bonds, usually through complementary base pairing, usually through hydrogen bond formation. As used herein, a probe may include natural (i.e., A, G, C, or T) or modified bases (7-deazaguanosine, inosine, etc.). In addition, the bases in a probe may be joined by a linkage other than a phosphodiester bond, so long as it does not functionally

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interfere with hybridization. Thus, e.g., probes may be peptide nucleic acids in which the constituent bases are joined by peptide bonds rather than phosphodiester linkages. It will be understood by one of skill in the art that probes may bind target sequences lacking complete complementarity with the probe sequence depending upon the stringency of the hybridization conditions. The probes are preferably directly labeled as with isotopes, chromophores, lumiphores, chromogens, or indirectly labeled such as with biotin to which a streptavidin complex may later bind. By assaying for the presence or absence of the probe, one can detect the presence or absence of the select sequence or subsequence. Diagnosis or prognosis may be based at the genomic level, or at the level of RNA or protein expression.

The term "recombinant" when used with reference, e.g., to a cell, or nucleic acid, protein, or vector, indicates that the cell, nucleic acid, protein or vector, has been modified by the introduction of a heterologous nucleic acid or protein or the alteration of a native nucleic acid or protein, or that the cell is derived from a cell so modified. Thus, e.g., recombinant cells express genes that are not found within the native (non-recombinant) form of the cell or express native genes that are otherwise abnormally expressed, under expressed or not expressed at all. By the term "recombinant nucleic acid" herein is meant nucleic acid, originally formed in vitro, in general, by the manipulation of nucleic acid, e.g., using polymerases and endonucleases, in a form not normally found in nature. In this manner, operably linkage of different sequences is achieved. Thus an isolated nucleic acid, in a linear form, or an expression vector formed in vitro by ligating DNA molecules that are not normally joined, are both considered recombinant for the purposes of this invention. It is understood that once a recombinant nucleic acid is made and reintroduced into a host cell or organism, it will replicate non-recombinantly, i.e., using the in vivo cellular machinery of the host cell rather than in vitro manipulations; however, such nucleic acids, once produced recombinantly, although subsequently replicated non-recombinantly, are still considered recombinant for the purposes of the invention. Similarly, a "recombinant protein" is a protein made using recombinant techniques, i.e., through the expression of a recombinant nucleic acid as depicted above.

The term "heterologous" when used with reference to portions of a nucleic acid indicates that the nucleic acid comprises two or more subsequences that are not normally found in the same relationship to each other in nature. For instance, the nucleic acid is typically recombinantly produced, having two or more sequences, e.g., from unrelated genes

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arranged to make a new functional nucleic acid, e.g., a promoter from one source and a coding region from another source. Similarly, a heterologous protein will often refer to two or more subsequences that are not found in the same relationship to each other in nature (e.g., a fusion protein).

A "promoter" is defined as an array of nucleic acid control sequences that direct transcription of a nucleic acid. As used herein, a promoter includes necessary nucleic acid sequences near the start site of transcription, such as, in the case of a polymerase II type promoter, a TATA element. A promoter also optionally includes distal enhancer or repressor elements, which can be located as much as several thousand base pairs from the start site of transcription. A "constitutive" promoter is a promoter that is active under most environmental and developmental conditions. An "inducible" promoter is a promoter that is active under environmental or developmental regulation. The term "operably linked" refers to a functional linkage between a nucleic acid expression control sequence (such as a promoter, or array of transcription factor binding sites) and a second nucleic acid sequence, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

An "expression vector" is a nucleic acid construct, generated recombinantly or synthetically, with a series of specified nucleic acid elements that permit transcription of a particular nucleic acid in a host cell. The expression vector can be part of a plasmid, virus, or nucleic acid fragment. Typically, the expression vector includes a nucleic acid to be transcribed operably linked to a promoter.

The phrase "selectively (or specifically) hybridizes to" refers to the binding, duplexing, or hybridizing of a molecule only to a particular nucleotide sequence under stringent hybridization conditions when that sequence is present in a complex mixture (e.g., total cellular or library DNA or RNA).

The phrase "stringent hybridization conditions" refers to conditions under which a probe will hybridize to its target subsequence, typically in a complex mixture of nucleic acids, but to no other sequences. Stringent conditions are sequence-dependent and will be different in different circumstances. Longer sequences hybridize specifically at higher temperatures. An extensive guide to the hybridization of nucleic acids is found "Overview of principles of hybridization and the strategy of nucleic acid assays" in Tijssen (1993)

Hybridization with Nucleic Probes (Techniques in Biochemistry and Molecular Biology vol.

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24) Elsevier. Generally, stringent conditions are selected to be about 5-10° C lower than the thermal melting point (Tm) for the specific sequence at a defined ionic strength pH. The Tm is the temperature (under defined ionic strength, pH, and nucleic concentration) at which 50% of the probes complementary to the target hybridize to the target sequence at equilibrium (as the target sequences are present in excess, at T_m, 50% of the probes are occupied at equilibrium). Stringent conditions will be those in which the salt concentration is less than about 1.0 M sodium ion, typically about 0.01 to 1.0 M sodium ion concentration (or other salts) at pH 7.0 to 8.3 and the temperature is at least about 30°C for short probes (e.g., 10 to 50 nucleotides) and at least about 60° C for long probes (e.g., greater than 50 nucleotides). Stringent conditions may also be achieved with the addition of destabilizing agents such as formamide. For selective or specific hybridization, a positive signal is at least two times background, preferably 10 times background hybridization. Exemplary stringent hybridization conditions can be as following: 50% formamide, 5x SSC, and 1% SDS, incubating at 42° C, or, 5x SSC, 1% SDS, incubating at 65° C, with wash in 0.2x SSC, and 0.1% SDS at 65° C. For PCR, a temperature of about 36° C is typical for low stringency amplification, although annealing temperatures may vary between about 32° C and 48° C depending on primer length. For high stringency PCR amplification, a temperature of about 62° C is typical, although high stringency annealing temperatures can range from about 50-65° C. depending on the primer length and specificity. Typical cycle conditions for both high and low stringency amplifications include a denaturation phase of 90-95° C for 30-120 sec, an annealing phase lasting 30-120 sec, and an extension phase of about 72° C for 1-2 min. Protocols and guidelines for low and high stringency amplification reactions are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press, N.Y.

Nucleic acids that do not hybridize to each other under stringent conditions are still substantially identical if the polypeptides which they encode are substantially identical. This occurs, e.g., when a copy of a nucleic acid is created using the maximum codon degeneracy permitted by the genetic code. In such cases, the nucleic acids typically hybridize under moderately stringent hybridization conditions. Exemplary "moderately stringent hybridization conditions in a buffer of 40% formamide, 1 M NaCl, 1% SDS at 37° C, and a wash in 1X SSC at 45° C. A positive hybridization is at least twice

background. Those of ordinary skill will readily recognize that alternative hybridization and wash conditions can be utilized to provide conditions of similar stringency. Additional guidelines for determining hybridization parameters are provided in numerous references, e.g., Ausubel, et al. (eds. 1991 and supplements) <u>Current Protocols in Molecular Biology</u>

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The phrase "functional effects" in the context of assays for testing compounds that modulate activity of a prostate cancer protein includes the determination of a parameter that is indirectly or directly under the influence of the prostate cancer protein or nucleic acid, e.g., a functional, physical, or chemical effect, such as the ability to decrease prostate proliferation (malignant or non-malignant). It includes ligand binding activity; cell growth on soft agar; anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells. "Functional effects" include in vitro, in vivo, and ex vivo activities.

By "determining the functional effect" is meant assaying for a compound that increases or decreases a parameter that is indirectly or directly under the influence of a prostate cancer protein sequence, e.g., functional, enzymatic, physical and chemical effects. Such functional effects can be measured by means known to those skilled in the art, e.g., changes in spectroscopic characteristics (e.g., fluorescence, absorbance, refractive index), hydrodynamic (e.g., shape), chromatographic, or solubility properties for the protein, measuring inducible markers or transcriptional activation of the prostate cancer protein; measuring binding activity or binding assays, e.g., binding to antibodies or other ligands, and measuring cellular proliferation. Determination of the functional effect of a compound on prostate cancer can also be performed using prostate cancer assays known to those of skill in the art such as an in vitro assays, e.g., cell growth on soft agar; anchorage dependence; contact inhibition and density limitation of growth; cellular proliferation; cellular transformation; growth factor or serum dependence; tumor specific marker levels; invasiveness into Matrigel; tumor growth and metastasis in vivo; mRNA and protein expression in cells undergoing metastasis, and other characteristics of prostate cancer cells. The functional effects can be evaluated by many means known to those skilled in the art, e.g., microscopy for quantitative or qualitative measures of alterations in morphological features, measurement of changes in RNA or protein levels for prostate cancer-associated sequences,

measurement of RNA stability, identification of downstream or reporter gene expression (CAT, luciferase, β-gal, GFP, and the like), e.g., via chemiluminescence, fluorescence, colorimetric reactions, antibody binding, inducible markers, and ligand binding assays.

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"Inhibitors", "activators", and "modulators" of prostate cancer polynucleotide and polypeptide sequences are used to refer to activating, inhibitory, or modulating molecules or compounds identified using in vitro and in vivo assays of prostate cancer polynucleotide and polypeptide sequences. Inhibitors are compounds that, e.g., bind to, partially or totally block activity, decrease, prevent, delay activation, inactivate, desensitize, or down regulate the activity or expression of prostate cancer proteins, e.g., antagonists. Antisense nucleic acids may seem to inhibit expression and subsequent function of the protein. "Activators" are compounds that increase, open, activate, facilitate, enhance activation, sensitize, agonize, or up regulate prostate cancer protein activity. Inhibitors, activators, or modulators also include genetically modified versions of prostate cancer proteins, e.g., versions with altered activity, as well as naturally occurring and synthetic ligands, antagonists, agonists, antibodies, small chemical molecules and the like. Such assays for inhibitors and activators include, e.g., expressing the prostate cancer protein in vitro, in cells, or cell membranes, applying putative modulator compounds, and then determining the functional effects on activity, as described above. Activators and inhibitors of prostate cancer can also be identified by incubating prostate cancer cells with the test compound and determining increases or decreases in the expression of 1 or more prostate cancer proteins, e.g., 1, 2, 3, 4, 5, 10, 15, 20, 25, 30, 40, 50 or more prostate cancer proteins, such as prostate cancer proteins encoded by the sequences set out in Tables 1A-4.

Samples or assays comprising prostate cancer proteins that are treated with a potential activator, inhibitor, or modulator are compared to control samples without the inhibitor, activator, or modulator to examine the extent of inhibition. Control samples (untreated with inhibitors) are assigned a relative protein activity value of 100%. Inhibition of a polypeptide is achieved when the activity value relative to the control is about 80%, preferably 50%, more preferably 25-0%. Activation of a prostate cancer polypeptide is achieved when the activity value relative to the control (untreated with activators) is 110%, more preferably 150%, more preferably 200-500% (i.e., two to five fold higher relative to the control), more preferably 1000-3000% higher.

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The phrase "changes in cell growth" refers to a change in cell growth and proliferation characteristics in vitro or in vivo, such as cell viability, formation of foci, anchorage independence, semi-solid or soft agar growth, changes in contact inhibition and density limitation of growth, loss of growth factor or serum requirements, changes in cell morphology, gaining or losing immortalization, gaining or losing tumor specific markers, ability to form or suppress tumors when injected into suitable animal hosts, and/or immortalization of the cell. See, e.g., pp. 231-241 in Freshney (1994) <u>Culture of Animal Cells: A Manual of Basic Technique</u> (3d ed.) Wiley-Liss.

"Tumor cell" refers to precancerous, cancerous, and/or normal cells in a tumor.

"Cancer cells," "transformed" cells, or "transformation" in tissue culture, refers to spontaneous or induced phenotypic changes that do not necessarily involve the uptake of new genetic material. Although transformation can arise from infection with a transforming virus and incorporation of new genomic DNA, or uptake of exogenous DNA, it can also arise spontaneously or following exposure to a carcinogen, thereby mutating an endogenous gene. Transformation is associated with phenotypic changes, such as immortalization of cells, aberrant growth control, nonmorphological changes, and/or malignancy. See, Freshney (2001) Culture of Animal Cells: A Manual of Basic Technique (4th ed.) Wiley-Liss.

"Antibody" refers to a polypeptide comprising a framework region from an immunoglobulin gene or fragments thereof that specifically binds and recognizes an antigen. The recognized immunoglobulin genes include the kappa, lambda, alpha, gamma, delta, epsilon, and mu constant region genes, as well as the myriad immunoglobulin variable region genes. Light chains are classified as either kappa or lambda. Heavy chains are classified as gamma, mu, alpha, delta, or epsilon, which in turn define the immunoglobulin classes, IgG, IgM, IgA, IgD, and IgE, respectively. Typically, the antigen-binding region of an antibody or its functional equivalent will be most critical in specificity and affinity of binding. See Paul (ed. 1999) Fundamental Immunology (4th ed.) Raven.

An exemplary immunoglobulin (antibody) structural unit comprises a tetramer. Each tetramer is composed of two identical pairs of polypeptide chains, each pair having one "light" (about 25 kD) and one "heavy" chain (about 50-70 kD). The N-terminus of each chain defines a variable region of about 100 to 110 or more amino acids primarily responsible for antigen recognition. The terms variable light chain (V_L) and variable heavy chain (V_H) refer to these light and heavy chains respectively.

Antibodies exist, e.g., as intact immunoglobulins or as a number of well-characterized fragments produced by digestion with various peptidases. Thus, e.g., pepsin digests an antibody below the disulfide linkages in the hinge region to produce F(ab)'2, a dimer of Fab which itself is a light chain joined to V_H-C_HI by a disulfide bond. The F(ab)'2 may be reduced under mild conditions to break the disulfide linkage in the hinge region, thereby converting the F(ab)'2 dimer into an Fab' monomer. The Fab' monomer is essentially Fab with part of the hinge region (see Paul (ed. 1993) Fundamental Immunology (3d ed.) Raven. While various antibody fragments are defined in terms of the digestion of an intact antibody, one of skill will appreciate that such fragments may be synthesized de novo either chemically or by using recombinant DNA methodology. Thus, the term antibody, as used herein, also includes antibody fragments either produced by the modification of whole antibodies, or those synthesized de novo using recombinant DNA methodologies (e.g., single chain Fv) or those identified using phage display libraries (see, e.g., McCafferty, et al.(1990) Nature 348:552-554.

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For preparation of antibodies, e.g., recombinant, monoclonal, or polyclonal antibodies, many technique known in the art can be used (see, e.g., Kohler and Milstein (1975) Nature 256:495-497; Kozbor, et al. (1983) Immunology Today 4:72; pp. 77-96 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; Coligan (1991) Current Protocols in Immunology Lippincott; Harlow and Lane (1988) Antibodies: A Laboratory Manual CSH Press; and Goding (1986) Monoclonal Antibodies: Principles and Practice (2d ed.) Academic Press. Techniques for the production of single chain antibodies (U.S. Patent 4,946,778) can be adapted to produce antibodies to polypeptides of this invention. Also, transgenic mice, or other organisms such as other mammals, may be used to express humanized antibodies. Alternatively, phage display technology can be used to identify antibodies and heteromeric Fab fragments that specifically bind to selected antigens (see, e.g., McCafferty, et al. (1990) Nature 348:552-554; Marks, et al. (1992) Biotechnology 10:779-783).

A "chimeric antibody" is an antibody molecule in which (a) the constant region, or a portion thereof, is altered, replaced or exchanged so that the antigen binding site (variable region) is linked to a constant region of a different or altered class, effector function and/or species, or an entirely different molecule which confers new properties to the chimeric antibody, e.g., an enzyme, toxin, hormone, growth factor, drug, etc.; or (b) the variable

region, or a portion thereof, is altered, replaced or exchanged with a variable region having a different or altered antigen specificity.

Identification of prostate cancer-associated sequences

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In one aspect, the expression levels of genes are determined in different patient samples for which diagnosis information is desired, to provide expression profiles. An expression profile of a particular sample is essentially a "fingerprint" of the state of the sample; while two states may have a particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is characteristic of the state of the cell. That is, normal tissue (e.g., normal prostate or other tissue) may be distinguished from pathological prostate cells, e.g., cancerous or metastatic cancerous tissue of the prostate, or prostate cancer tissue or metastatic prostate cancerous tissue can be compared with tissue samples of prostate and other tissues from surviving cancer patients. By comparing expression profiles of tissue in known different prostate cancer states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained.

The identification of sequences that are differentially expressed in prostate cancer versus non-prostate cancer tissue allows the use of this information in a number of ways. For example, a particular treatment regime may be evaluated: does a chemotherapeutic drug act to down-regulate prostate cancer or other proliferative disorders, and thus tumor growth or recurrence, in a particular patient. Alternatively, a treatment step may induce other markers which may be used as targets to destroy tumor cells. Similarly, diagnosis and treatment outcomes may be done or confirmed by comparing patient samples with the known expression profiles. Maliganant disease may be compared to non-malignant conditions. Metastatic tissue can also be analyzed to determine the stage of prostate cancer in the tissue, or origin of primary tumor, e.g., metastasis from a remote primary site. Furthermore, these gene expression profiles (or individual genes) allow screening of drug candidates with an eye to mimicking or altering a particular expression profile; e.g., screening can be done for drugs that suppress the prostate cancer expression profile. This may be done by making biochips comprising sets of the important prostate cancer genes, which can then be used in these screens. These methods can also be done on the protein basis; that is, protein expression levels of the prostate cancer proteins can be evaluated for diagnostic purposes or to screen

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candidate agents. In addition, the prostate cancer nucleic acid sequences can be administered for gene therapy purposes, including the administration of antisense nucleic acids, or the prostate cancer proteins (including antibodies and other modulators thereof) administered as therapeutic drugs.

Thus the present invention provides nucleic acid and protein sequences that are differentially expressed in prostate cancer relative to normal tissues and/or non-malignant disease, or in different types of related diseases, herein termed "prostate cancer sequences." As outlined below, prostate cancer sequences include those that are up-regulated (i.e., expressed at a higher level) in prostate cancer, as well as those that are down-regulated (i.e., expressed at a lower level). In a preferred embodiment, the prostate cancer sequences are from humans; however, as will be appreciated by those in the art, prostate cancer sequences from other organisms may be useful in animal models of disease and drug evaluation; thus, other prostate cancer sequences are provided, from vertebrates, including mammals, including rodents (rats, mice, hamsters, guinea pigs, etc.), primates, farm animals (including sheep, goats, pigs, cows, horses, etc.) and pets, e.g., (dogs, cats, etc.). Prostate cancer sequences from other organisms may be obtained using the techniques outlined below.

Prostate cancer sequences can include both nucleic acid and amino acid sequences. As will be appreciated by those in the art and is more fully outlined below, prostate cancer nucleic acid sequences are useful in a variety of applications, including diagnostic applications, which will detect naturally occurring nucleic acids, as well as screening applications; e.g., biochips comprising nucleic acid probes or PCR microtiter plates with selected probes to the prostate cancer sequences can be generated.

A prostate cancer sequence can be initially identified by substantial nucleic acid and/or amino acid sequence homology to the prostate cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions.

For identifying prostate cancer-associated sequences, the prostate cancer screen typically includes comparing genes identified in different tissues, e.g., normal and cancerous tissues, or tumor tissue samples from patients who have metastatic disease vs. non metastatic tissue. Other suitable tissue comparisons include comparing prostate cancer samples with metastatic cancer samples from other cancers, such as lung, breast, gastrointestinal cancers,

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ovarian, etc. Samples of different stages of prostate cancer, e.g., survivor tissue, drug resistant states, and tissue undergoing metastasis, are applied to biochips comprising nucleic acid probes. The samples are first microdissected, if applicable, and treated as is known in the art for the preparation of mRNA. Suitable biochips are commercially available, e.g., from Affymetrix. Gene expression profiles are generated and the data analyzed.

In one embodiment, the genes showing changes in expression as between normal and disease states are compared to genes expressed in other normal tissues, preferably normal prostate, but also including, and not limited to lung, heart, brain, liver, breast, kidney, muscle, colon, small intestine, large intestine, spleen, bone, and placenta. In a preferred embodiment, those genes identified during the prostate cancer screen that are expressed in a significant amount in other tissues are removed from the profile, although in some embodiments, this is not necessary. That is, when screening for drugs, it is usually preferable that the target be disease specific, to minimize possible side effects on other organs were there expression.

In a preferred embodiment, prostate cancer sequences are those that are up-regulated in prostate cancer or related conditions; that is, the expression of these genes is higher in the prostate cancer tissue as compared to non-cancerous tissue. "Up-regulation" as used herein often means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred. Another embodiment is directed to sequences up-regulated in non-malignant conditions relative to normal.

Unigene cluster identification numbers and accession numbers herein are for the GenBank sequence database and the sequences of the accession numbers are hereby expressly incorporated by reference. GenBank is known in the art, see, e.g., Benson, et al. (1998) Nucleic Acids Research 26:1-7 and http://www.ncbi.nlm.nih.gov/. Sequences are also available in other databases, e.g., European Molecular Biology Laboratory (EMBL) and DNA Database of Japan (DDBI). U.S. Patent Application N. 09/687,576 and 09/976,858 (-001-3) further disclose related sequences, compositions, and methods of diagnosis and treatment of prostate cancer and related conditions and are hereby expressly incorporated by reference.

In another preferred embodiment, prostate cancer sequences are those that are downregulated in the prostate cancer; that is, the expression of these genes is lower in prostate cancer tissue as compared to non-cancerous tissue. "Down-regulation" as used herein often

means at least about a two-fold change, preferably at least about a three fold change, with at least about five-fold or higher being preferred.

Informatics

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The ability to identify genes that are over or under expressed in prostate cancer can additionally provide high-resolution, high-sensitivity datasets which can be used in the areas of diagnostics, therapeutics, drug development, pharmacogenetics, protein structure, biosensor development, and other related areas. For example, the expression profiles can be used in diagnostic or prognostic evaluation of patients with prostate cancer. Or as another example, subcellular toxicological information can be generated to better direct drug structure and activity correlation (see Anderson, Pharmaceutical Proteomics: Targets, Mechanism, and Function, paper presented at the IBC Proteomics conference, Coronado, CA (June 11-12, 1998)). Subcellular toxicological information can also be utilized in a biological sensor device to predict the likely toxicological effect of chemical exposures and likely tolerable exposure thresholds (see U.S. Patent No. 5,811,231). Similar advantages accrue from datasets relevant to other biomolecules and bioactive agents (e.g., nucleic acids, saccharides, lipids, drugs, and the like).

Thus, in another embodiment, the present invention provides a database that includes at least one set of assay data. The data contained in the database is acquired, e.g., using array analysis either singly or in a library format. The database can be in a form in which data can be maintained and transmitted, but is preferably an electronic database. The electronic database of the invention can be maintained on an electronic device allowing for the storage of and access to the database, such as a personal computer, but is preferably distributed on a wide area network, such as the World Wide Web.

The focus of the present section on databases that include peptide sequence data is for clarity of illustration only. It will be apparent to those of skill in the art that similar databases can be assembled for assay data acquired using an assay of the invention.

The compositions and methods for identifying and/or quantitating the relative and/or absolute abundance of a variety of molecular and macromolecular species from a biological sample undergoing prostate cancer, i.e., the identification of prostate cancer-associated sequences described herein, provide an abundance of information, which can be correlated with pathological conditions, predisposition to disease, drug testing, therapeutic monitoring,

gene-disease causal linkages, identification of correlates of immunity and physiological status, among others. Although the data generated from the assays of the invention is suited for manual review and analysis, in a preferred embodiment, prior data processing using high-speed computers is utilized.

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An array of methods for indexing and retrieving biomolecular information is known in the art. For example, U.S. Patents 6,023,659 and 5,966,712 disclose a relational database system for storing biomolecular sequence information in a manner that allows sequences to be catalogued and searched according to one or more protein function hierarchies. U.S. Patent 5,953,727 discloses a relational database having sequence records containing information in a format that allows a collection of partial-length DNA sequences to be catalogued and searched according to association with one or more sequencing projects for obtaining full-length sequences from the collection of partial length sequences. U.S. Patent 5,706,498 discloses a gene database retrieval system for making a retrieval of a gene sequence similar to a sequence data item in a gene database based on the degree of similarity between a key sequence and a target sequence. U.S. Patent 5,538,897 discloses a method using mass spectroscopy fragmentation patterns of peptides to identify amino acid sequences in computer databases by comparison of predicted mass spectra with experimentally-derived mass spectra using a closeness-of-fit measure. U.S. Patent 5,926,818 discloses a multidimensional database comprising a functionality for multi-dimensional data analysis described as on-line analytical processing (OLAP), which entails the consolidation of projected and actual data according to more than one consolidation path or dimension. U.S. Patent 5.295.261 reports a hybrid database structure in which the fields of each database record are divided into two classes, navigational and informational data, with navigational fields stored in a hierarchical topological map which can be viewed as a tree structure or as the merger of two or more such tree structures.

See also Mount, et al. (2001) <u>Bioinformatics</u> CSH Press; Durbin, et al. (eds. 1999) <u>Biological Sequence Analysis: Probabilistic Models of Proteins and Nucleic Acids</u> Cambridge Univ. Press; Baxevanis and Oeullette (eds., 1998) <u>Bioinformatics: A Practical Guide to the Analysis of Genes and Proteins</u> Wiley-Liss; Rashidi and Buehler (1999) <u>Bioinformatics: Basic Applications in Biological Science and Medicine</u> CRC Press; Setubal, et al. (eds. 1997) <u>Introduction to Computational Molecular Biology</u> Brooks/Cole; Misener and Krawetz (eds. 2000) <u>Bioinformatics</u>: Methods and Protocols Human Press; Higgins and

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Taylor (eds. 2000) <u>Bioinformatics: Sequence, Structure, and Databanks: A Practical Approach</u> Oxford Univ. Press; Brown (2001) <u>Bioinformatics: A Biologist's Guide to Biocomputing and the Internet</u> Eaton Pub; Han and Kamber (2000) <u>Data Mining: Concepts and Techniques</u> Kaufmann Pub.; and Waterman (1995) <u>Introduction to Computational Biology; Maps, Sequences, and Genomes</u> Chap and Hall.

The present invention provides a computer database comprising a computer and software for storing in computer-retrievable form assay data records cross-tabulated, e.g., with data specifying the source of the target-containing sample from which each sequence specificity record was obtained.

In an exemplary embodiment, at least one of the sources of target-containing sample is from a control tissue sample known to be free of pathological disorders. In a variation, at least one of the sources is a known pathological tissue specimen, e.g., a neoplastic lesion or another tissue specimen to be analyzed for prostate cancer. In another variation, the assay records cross-tabulate one or more of the following parameters for each target species in a sample: (1) a unique identification code, which can include, e.g., a target molecular structure and/or characteristic separation coordinate (e.g., electrophoretic coordinates); (2) sample source; and (3) absolute and/or relative quantity of the target species present in the sample.

The invention also provides for the storage and retrieval of a collection of target data in a computer data storage apparatus, which can include magnetic disks, optical disks, magneto-optical disks, DRAM, SRAM, SGRAM, SDRAM, RDRAM, DDR RAM, magnetic bubble memory devices, and other data storage devices, including CPU registers and on-CPU data storage arrays. Typically, the target data records are stored as a bit pattern in an array of magnetic domains on a magnetizable medium or as an array of charge states or transistor gate states, such as an array of cells in a DRAM device (e.g., each cell comprised of a transistor and a charge storage area, which may be on the transistor). In one embodiment, the invention provides such storage devices, and computer systems built therewith, comprising a bit pattern encoding a protein expression fingerprint record comprising unique identifiers for at least 10 target data records cross-tabulated with target source.

When the target is a peptide or nucleic acid, the invention preferably provides a method for identifying related peptide or nucleic acid sequences, comprising performing a computerized comparison between a peptide or nucleic acid sequence assay record stored in or retrieved from a computer storage device or database and at least one other sequence. The

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comparison can include a sequence analysis or comparison algorithm or computer program embodiment thereof (e.g., FASTA, TFASTA, GAP, BESTFIT) and/or the comparison may be of the relative amount of a peptide or nucleic acid sequence in a pool of sequences determined from a polypeptide or nucleic acid sample of a specimen.

The invention also preferably provides a magnetic disk, such as an IBM-compatible (DOS, Windows, Windows95/98/2000, Windows NT, OS/2) or other format (e.g., Linux, SunOS, Solaris, ADX, SCO Unix, VMS, MV, Macintosh, etc.) floppy diskette or hard (fixed, Winchester) disk drive, comprising a bit pattern encoding data from an assay of the invention in a file format suitable for retrieval and processing in a computerized sequence analysis, comparison, or relative quantitation method.

The invention also provides a network, comprising a plurality of computing devices linked via a data link, such as an Ethernet cable (coax or 10BaseT), telephone line, ISDN line, wireless network, optical fiber, or other suitable signal transmission medium, whereby at least one network device (e.g., computer, disk array, etc.) comprises a pattern of magnetic domains (e.g., magnetic disk) and/or charge domains (e.g., an array of DRAM cells) composing a bit pattern encoding data acquired from an assay of the invention.

The invention also provides a method for transmitting assay data that includes generating an electronic signal on an electronic communications device, such as a modem, ISDN terminal adapter, DSL, cable modem, ATM switch, or the like, wherein the signal includes (in native or encrypted format) a bit pattern encoding data from an assay or a database comprising a plurality of assay results obtained by the method of the invention.

In a preferred embodiment, the invention provides a computer system for comparing a query target to a database containing an array of data structures, such as an assay result obtained by the method of the invention, and ranking database targets based on the degree of identity and gap weight to the target data. A central processor is preferably initialized to load and execute the computer program for alignment and/or comparison of the assay results. Data for a query target is entered into the central processor via an I/O device. Execution of the computer program results in the central processor retrieving the assay data from the data file, which comprises a binary description of an assay result.

The target data or record and the computer program can be transferred to secondary memory, which is typically random access memory (e.g., DRAM, SRAM, SGRAM, or SDRAM). Targets are ranked according to the degree of correspondence between a selected

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assay characteristic (e.g., binding to a selected affinity moiety) and the same characteristic of the query target and results are output via an I/O device. For example, a central processor can be a conventional computer (e.g., Intel Pentium, PowerPC, Alpha, PA-8000, SPARC, MIPS 4400, MIPS 10000, VAX, etc.); a program can be a commercial or public domain molecular biology software package (e.g., UWGCG Sequence Analysis Software, Darwin); a data file can be an optical or magnetic disk, a data server, a memory device (e.g., DRAM, SRAM, SGRAM, SDRAM, EPROM, bubble memory, flash memory, etc.); an I/O device can be a terminal comprising a video display and a keyboard, a modem, an ISDN terminal adapter, an Ethernet port, a punched card reader, a magnetic strip reader, or other suitable I/O device.

The invention also preferably provides the use of a computer system, such as that described above, which comprises: (1) a computer; (2) a stored bit pattern encoding a collection of peptide sequence specificity records obtained by the methods of the invention, which may be stored in the computer; (3) a comparison target, such as a query target; and (4) a program for alignment and comparison, typically with rank-ordering of comparison results on the basis of computed similarity values.

Characteristics of prostate cancer-associated proteins

Prostate cancer proteins of the present invention may be classified as secreted proteins, transmembrane proteins, or intracellular proteins. In one embodiment, the prostate cancer protein is an intracellular protein. Intracellular proteins may be found in the cytoplasm and/or in the nucleus. Intracellular proteins are involved in all aspects of cellular function and replication (including, e.g., signaling pathways); aberrant expression of such proteins often results in unregulated or disregulated cellular processes (see, e.g., Alberts (ed. 1994) Molecular Biology of the Cell (3d ed.) Garland. For example, many intracellular proteins have enzymatic activity such as protein kinase activity, protein phosphatase activity, proteins activity, nucleotide cyclase activity, polymerase activity and the like. Intracellular proteins also serve as docking proteins that are involved in organizing complexes of proteins, or targeting proteins to various subcellular localizations, and are involved in maintaining the structural integrity of organelles.

An increasingly appreciated concept in characterizing proteins is the presence in the proteins of one or more structural motifs for which defined functions have been attributed. In

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addition to the highly conserved sequences found in the enzymatic domain of proteins, highly conserved sequences have been identified in proteins that are involved in protein-protein interaction. For example, Src-homology-2 (SH2) domains bind tyrosine-phosphorylated targets in a sequence dependent manner. PTB domains, which are distinct from SH2 domains, also bind tyrosine phosphorylated targets. SH3 domains bind to proline-rich targets. In addition, PH domains, tetratricopeptide repeats and WD domains to name only a few, have been shown to mediate protein-protein interactions. Some of these may also be involved in binding to phospholipids or other second messengers. As will be appreciated by one of ordinary skill in the art, these motifs can be identified on the basis of amino acid sequence; thus, an analysis of the sequence of proteins may provide insight into both the enzymatic potential of the molecule and/or molecules with which the protein may associate. One useful database is Pfam (protein families), which is a large collection of multiple sequence alignments and hidden Markov models covering many common protein domains. Versions are available via the internet from Washington University in St. Louis, the Sanger Center in England, and the Karolinska Institute in Sweden (see, e.g., Bateman, et al. (2000) Nuc. Acids Res. 28:263-266; Sonnhammer, et al. (1997) Proteins 28:405-420; Bateman, et al. (1999) Nuc. Acids Res. 27:260-262; and Sonnhammer, et al. (1998) Nuc. Acids Res. 26:320-322.

In another embodiment, the prostate cancer sequences are transmembrane proteins. Transmembrane proteins are molecules that span a phospholipid bilayer of a cell. They may have an intracellular domain, an extracellular domain, or both. The intracellular domains of such proteins may have a number of functions including those already described for intracellular proteins. For example, the intracellular domain may have enzymatic activity and/or may serve as a binding site for additional proteins. Frequently the intracellular domain of transmembrane proteins serves both roles. For example certain receptor tyrosine kinases have both protein kinase activity and SH2 domains. In addition, autophosphorylation of tyrosines on the receptor molecule itself, creates binding sites for additional SH2 domain containing proteins.

Transmembrane proteins may contain from one to many transmembrane domains.

For example, receptor tyrosine kinases, certain cytokine receptors, receptor guanylyl cyclases and receptor serine/threonine protein kinases contain a single transmembrane domain.

However, various other proteins including channels and adenylyl cyclases contain numerous

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transmembrane domains. Many important cell surface receptors such as G protein coupled receptors (GPCRs) are classified as "seven transmembrane domain" proteins, as they contain 7 membrane spanning regions. Characteristics of transmembrane domains include approximately 17 consecutive hydrophobic amino acids that may be followed by charged amino acids. Therefore, upon analysis of the amino acid sequence of a particular protein, the localization and number of transmembrane domains within the protein may be predicted (see, e.g., PSORT web site http://psort.nibb.ac.jp/). Important transmembrane protein receptors include, but are not limited to the insulin receptor, insulin-like growth factor receptor, human growth hormone receptor, glucose transporters, transferrin receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, low density lipoprotein receptor, epidermal growth factor receptor, and interleukin receptors, e.g., IL-1 receptor, IL-2 receptor, etc.

The extracellular domains of transmembrane proteins are diverse; however, conserved motifs are found repeatedly among various extracellular domains. Conserved structure and/or functions have been ascribed to different extracellular motifs. Many extracellular domains are involved in binding to other molecules. In one aspect, extracellular domains are found on receptors. Factors that bind the receptor domain include circulating ligands, which may be peptides, proteins, or small molecules such as adenosine and the like. For example, growth factors such as EGF, FGF, and PDGF are circulating growth factors that bind to their cognate receptors to initiate a variety of cellular responses. Other factors include cytokines, mitogenic factors, neurotrophic factors and the like. Extracellular domains also bind to cell-associated molecules. In this respect, they mediate cell-cell interactions. Cell-associated ligands can be tethered to the cell, e.g., via a glycosylphosphatidylinositol (GPI) anchor, or may themselves be transmembrane proteins. Extracellular domains also associate with the extracellular matrix and contribute to the maintenance of the cell structure.

Prostate cancer proteins that are transmembrane are particularly preferred in the present invention as they are readily accessible targets for immunotherapeutics, as are described herein. In addition, as outlined below, transmembrane proteins can be also useful in imaging modalities. Antibodies may be used to label such readily accessible proteins in situ. Alternatively, antibodies can also label intracellular proteins, in which case samples are typically permeablized to provide access to intracellular proteins. In addition, some membrane proteins can be processed to release a soluble protein, or to expose a residual

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fragment. Released soluble proteins may be useful diagnostic markers, processed residual protein fragments may be useful prostate markers of disease.

It will also be appreciated by those in the art that a transmembrane protein can be made soluble by removing transmembrane sequences, e.g., through recombinant methods. Furthermore, transmembrane proteins that have been made soluble can be made to be secreted through recombinant means by adding an appropriate signal sequence.

In another embodiment, the prostate cancer proteins are secreted proteins; the secretion of which can be either constitutive or regulated. These proteins may have a signal peptide or signal sequence that targets the molecule to the secretory pathway. Secreted proteins are involved in numerous physiological events; by virtue of their circulating nature, they often serve to transmit signals to various other cell types. The secreted protein may function in an autocrine manner (acting on the cell that secreted the factor), a paracrine manner (acting on cells in close proximity to the cell that secreted the factor), an endocrine manner (acting on cells at a distance, e.g., secretion into the blood stream), or an exocrine manner (secretion, e.g., through a duct or to adjacent epithelial surface as sweat glands, sebaceous glands, pancreatic ducts, lacrimal glands, mammary glands, sax producing glands of the ear, etc.). Thus secreted molecules find use in modulating or altering numerous aspects of physiology. Prostate cancer proteins that are secreted proteins are particularly preferred in the present invention as they serve as good targets for diagnostic markers, e.g., for blood, plasma, serum, or stool tests. Those which are enzymes may be antibody or small molecule targets. Others may be useful as vaccine targets, e.g., via CTL mechanisms.

Use of prostate cancer nucleic acids

As described above, prostate cancer sequence is initially identified by substantial nucleic acid and/or amino acid sequence homology or linkage to the prostate cancer sequences outlined herein. Such homology can be based upon the overall nucleic acid or amino acid sequence, and is generally determined as outlined below, using either homology programs or hybridization conditions. Typically, linked sequences on a mRNA are found on the same molecule.

The prostate cancer nucleic acid sequences of the invention, e.g., the sequences in Tables 1A-4, can be fragments of larger genes, i.e., they are nucleic acid segments. "Genes" in this context includes coding regions, non-coding regions, and mixtures of coding and non-

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coding regions. Accordingly, as will be appreciated by those in the art, using the sequences provided herein, extended sequences, in either direction, of the prostate cancer genes can be obtained, using techniques well known in the art for cloning either longer sequences or the full length sequences; see Ausubel, et al., supra. Much can be done by informatics and many sequences can be clustered to include multiple sequences corresponding to a single gene, e.g., systems such as UniGene (see, http://www.ncbi.nlm.nih.gov/UniGene/).

Once the prostate cancer nucleic acid is identified, it can be cloned and, if necessary, its constituent parts recombined to form the entire prostate cancer nucleic acid coding regions or the entire mRNA sequence. Once isolated from its natural source, e.g., contained within a plasmid or other vector or excised therefrom as a linear nucleic acid segment, the recombinant prostate cancer nucleic acid can be further-used as a probe to identify and isolate other prostate cancer nucleic acids, e.g., extended coding regions. It can also be used as a "precursor" nucleic acid to make modified or variant prostate cancer nucleic acids and proteins.

The prostate cancer nucleic acids of the present invention are used in several ways. In a first embodiment, nucleic acid probes to the prostate cancer nucleic acids are made and attached to biochips to be used in screening and diagnostic methods, as outlined below, or for administration, e.g., for gene therapy, vaccine, and/or antisense applications. Alternatively, the prostate cancer nucleic acids that include coding regions of prostate cancer proteins can be put into expression vectors for the expression of prostate cancer proteins, again for screening purposes or for administration to a patient.

In a preferred embodiment, nucleic acid probes to prostate cancer nucleic acids (both the nucleic acid sequences outlined in the figures and/or the complements thereof) are made. The nucleic acid probes attached to the biochip are designed to be substantially complementary to the prostate cancer nucleic acids, i.e., the target sequence (either the target sequence of the sample or to other probe sequences, e.g., in sandwich assays), such that hybridization of the target sequence and the probes of the present invention occurs. As outlined below, this complementarity need not be perfect; there may be base pair mismatches which will interfere with hybridization between the target sequence and the single stranded nucleic acids of the present invention. However, if the number of mutations is so great that no hybridization can occur under even the least stringent of hybridization conditions, the sequence is not a complementary target sequence. Thus, by "substantially complementary"

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herein is meant that the probes are sufficiently complementary to the target sequences to hybridize under normal reaction conditions, particularly high stringency conditions, as outlined herein.

A nucleic acid probe is generally single stranded but can be partially single and partially double stranded. The strandedness of the probe is dictated by the structure, composition, and properties of the target sequence. In general, the nucleic acid probes range from about 8 to about 100 bases long, with from about 10 to about 80 bases being preferred, and from about 30 to about 50 bases being particularly preferred. That is, generally whole genes are not used. In some embodiments, much longer nucleic acids can be used, up to hundreds of bases.

In a preferred embodiment, more than one probe per sequence is used, with either overlapping probes or probes to different sections of the target being used. That is, two, three, four or more probes, with three being preferred, are used to build in a redundancy for a particular target. The probes can be overlapping (i.e., have some sequence in common), or separate. In some cases, PCR primers may be used to amplify signal for higher sensitivity.

As will be appreciated by those in the art, nucleic acids can be attached or immobilized to a solid support in a wide variety of ways. By "immobilized" and grammatical equivalents herein is meant the association or binding between the nucleic acid probe and the solid support is sufficient to be stable under the conditions of binding, washing, analysis, and removal as outlined below. The binding can typically be covalent or non-covalent. By "non-covalent binding" and grammatical equivalents herein is meant one or more of electrostatic, hydrophilic, and hydrophobic interactions. Included in non-covalent binding is the covalent attachment of a molecule, such as, streptavidin to the support and the non-covalent binding of the biotinylated probe to the streptavidin. By "covalent binding" and grammatical equivalents herein is meant that the two moieties, the solid support and the probe, are attached by at least one bond, including sigma bonds, pi bonds and coordination bonds. Covalent bonds can be formed directly between the probe and the solid support or can be formed by a cross linker or by inclusion of a specific reactive group on either the solid support or the probe or both molecules. Immobilization may also involve a combination of covalent and non-covalent interactions.

In general, the probes are attached to the biochip in a wide variety of ways, as will be appreciated by those in the art. As described herein, the nucleic acids can either be

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synthesized first, with subsequent attachment to the biochip, or can be directly synthesized on the biochip.

The biochip comprises a suitable solid substrate. By "substrate" or "solid support" or other grammatical equivalents herein is meant a material that can be modified to contain discrete individual sites appropriate for the attachment or association of the nucleic acid probes and is amenable to at least one detection method. As will be appreciated by those in the art, the number of possible substrates are very large, and include, but are not limited to, glass and modified or functionalized glass, plastics (including acrylics, polystyrene and copolymers of styrene and other materials, polypropylene, polyethylene, polybutylene, polyurethanes, TeflonJ, etc.), polysaccharides, nylon or nitrocellulose, resins, silica or silicabased materials including silicon and modified silicon, carbon, metals, inorganic glasses, plastics, etc. In general, the substrates allow optical detection and do not appreciably fluoresce. A preferred substrate is described in WO0055627, herein incorporated by reference in its entirety.

Generally the substrate is planar, although as will be appreciated by those in the art, other configurations of substrates may be used as well. For example, the probes may be placed on the inside surface of a tube, for flow-through sample analysis to minimize sample volume. Similarly, the substrate may be flexible, such as a flexible foam, including closed cell foams made of particular plastics.

In a preferred embodiment, the surface of the biochip and the probe may be derivatized with chemical functional groups for subsequent attachment of the two. Thus, e.g., the biochip is derivatized with a chemical functional group including, but not limited to, amino groups, carboxy groups, oxo groups and thiol groups, with amino groups being particularly preferred. Using these functional groups, the probes can be attached using functional groups on the probes. For example, nucleic acids containing amino groups can be attached to surfaces comprising amino groups, e.g., using linkers as are known in the art; e.g., homo-or hetero-bifunctional linkers as are well known (see 1994 Pierce Chemical Company catalog, technical section on cross-linkers, pages 155-200). In addition, in some cases, additional linkers, such as alkyl groups (including substituted and heteroalkyl groups) may be used.

In this embodiment, oligonucleotides are synthesized as is known in the art, and then attached to the surface of the solid support. As will be appreciated by those skilled in the art,

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either the 5' or 3' terminus may be attached to the solid support, or attachment may be via an internal nucleoside.

In another embodiment, the immobilization to the solid support may be very strong, yet non-covalent. For example, biotinylated oligonucleotides can be made, which bind to surfaces covalently coated with streptavidin, resulting in attachment.

Alternatively, the oligonucleotides may be synthesized on the surface, as is known in the art. For example, photoactivation techniques utilizing photopolymerization compounds and techniques are used. In a preferred embodiment, the nucleic acids can be synthesized in situ, using well known photolithographic techniques, such as those described in WO 95/25116; WO 95/35505; U.S. Patent Nos. 5,700,637 and 5,445,934; and references cited within, all of which are expressly incorporated by reference; these methods of attachment form the basis of the Affymetrix GeneChip™ technology.

Often, amplification-based assays are performed to measure the expression level of prostate cancer-associated sequences. These assays are typically performed in conjunction with reverse transcription. In such assays, a prostate cancer-associated nucleic acid sequence acts as a template in an amplification reaction (e.g., Polymerase Chain Reaction, or PCR). In a quantitative amplification, the amount of amplification product will be proportional to the amount of template in the original sample. Comparison to appropriate controls provides a measure of the amount of prostate cancer-associated RNA. Methods of quantitative amplification are well known to those of skill in the art. Detailed protocols for quantitative PCR are provided, e.g., in Innis, et al. (1990) PCR Protocols: A Guide to Methods and Applications Academic Press.

In some embodiments, a TaqMan based assay is used to measure expression.

TaqMan based assays use a fluorogenic oligonucleotide probe that contains a 5' fluorescent dye and a 3' quenching agent. The probe hybridizes to a PCR product, but cannot itself be extended due to a blocking agent at the 3' end. When the PCR product is amplified in subsequent cycles, the 5' nuclease activity of the polymerase, e.g., AmpliTaq, results in the cleavage of the TaqMan probe. This cleavage separates the 5' fluorescent dye and the 3' quenching agent, thereby resulting in an increase in fluorescence as a function of amplification (see, e.g., literature provided by Perkin-Elmer, e.g., www2.perkin-elmer.com).

Other suitable amplification methods include, but are not limited to, ligase chain reaction (LCR) (see Wu and Wallace (1989) Genomics 4:560-569, Landegren, et al. (1988)

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Science 241:1077-1080, and Barringer, et al. (1990) Gene 89:117-122), transcription amplification (Kwoh, et al. (1989) Proc. Natl. Acad. Sci. USA 86:1173-1177), self-sustained sequence replication (Guatelli, et al. (1990) Proc. Nat. Acad. Sci. USA 87:1874-1878), dot PCR, and linker adapter PCR, etc.

Expression of prostate cancer proteins from nucleic acids

In a preferred embodiment, prostate cancer nucleic acids, e.g., encoding prostate cancer proteins are used to make a variety of expression vectors to express prostate cancer proteins which can then be used in screening assays, as described below. Expression vectors and recombinant DNA technology are well known to those of skill in the art (see, e.g., Ausubel, supra, and Fernandez and Hoeffler (eds. 1999) Gene Expression Systems Academic Press) and are used to express proteins. The expression vectors may be either self-replicating extrachromosomal vectors or vectors which integrate into a host genome. Generally, these expression vectors include transcriptional and translational regulatory nucleic acid operably linked to the nucleic acid encoding the prostate cancer protein. The term "control sequences" refers to DNA sequences used for the expression of an operably linked coding sequence in a particular host organism. Control sequences that are suitable for prokaryotes, e.g., include a promoter, optionally an operator sequence, and a ribosome binding site. Eukaryotic cells are known to utilize promoters, bolyadenylation signals, and enhancers.

Nucleic acid is "operably linked" when it is placed into a functional relationship with another nucleic acid sequence. For example, DNA for a presequence or secretory leader is operably linked to DNA for a polypeptide if it is expressed as a preprotein that participates in the secretion of the polypeptide; a promoter or enhancer is operably linked to a coding sequence if it affects the transcription of the sequence; a ribosome binding site is operably linked to a coding sequence if it is positioned so as to facilitate translation, and sequences may be operably linked when they are physically linked on the same molecule. Generally, "operably linked" means that the DNA sequences being linked are contiguous, and, in the case of a secretory leader, contiguous and in reading phase. However, enhancers do not have to be contiguous. Linking is typically accomplished by ligation at convenient restriction sites. If such sites do not exist, synthetic oligonucleotide adaptors or linkers are used in accordance with conventional practice. Transcriptional and translational regulatory nucleic acid will generally be appropriate to the host cell used to express the prostate cancer protein.

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Numerous types of appropriate expression vectors, and suitable regulatory sequences are known in the art for a variety of host cells.

In general, transcriptional and translational regulatory sequences may include, but are not limited to, promoter sequences, ribosomal binding sites, transcriptional start and stop sequences, translational start and stop sequences, and enhancer or activator sequences. In a preferred embodiment, the regulatory sequences include a promoter and transcriptional start and stop sequences.

Promoter sequences encode either constitutive or inducible promoters. The promoters may be either naturally occurring promoters or hybrid promoters. Hybrid promoters, which combine elements of more than one promoter, are also known in the art, and are useful in the present invention.

In addition, an expression vector may comprise additional elements. For example, the expression vector may have two replication systems, thus allowing it to be maintained in two organisms, e.g., in mammalian or insect cells for expression and in a prokaryotic host for cloning and amplification. Furthermore, for integrating expression vectors, the expression vector contains at least one sequence homologous to the host cell genome, and preferably two homologous sequences which flank the expression construct. The integrating vector may be directed to a specific locus in the host cell by selecting the appropriate homologous sequence for inclusion in the vector. Constructs for integrating vectors are well known in the art (e.g., Fernandez and Hoeffler, supra).

In addition, in a preferred embodiment, the expression vector contains a selectable marker gene to allow the selection of transformed host cells. Selection genes are well known in the art and will vary with the host cell used.

The prostate cancer proteins of the present invention are produced by culturing a host cell transformed with an expression vector containing nucleic acid encoding a prostate cancer protein, under the appropriate conditions to induce or cause expression of the prostate cancer protein. Conditions appropriate for prostate cancer protein expression will vary with the choice of the expression vector and the host cell, and will be easily ascertained by one skilled in the art through routine experimentation or optimization. For example, the use of constitutive promoters in the expression vector will require optimizing the growth and proliferation of the host cell, while the use of an inducible promoter requires the appropriate growth conditions for induction. In addition, in some embodiments, the timing of the harvest

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is important. For example, the baculoviral systems used in insect cell expression are lytic viruses, and thus harvest time selection can be crucial for product yield.

Appropriate host cells include yeast, bacteria, archaebacteria, fungi, and insect and animal cells, including mammalian cells. Of particular interest are Saccharomyces cerevisiae and other yeasts, E. coli, Bacillus subtilis, Sf9 cells, C129 cells, 293 cells, Neurospora, BHK, CHO, COS, HeLa cells, HUVEC (human umbilical vein endothelial cells), THP1 cells (a macrophage cell line) and various other human cells and cell lines.

In a preferred embodiment, the prostate cancer proteins are expressed in mammalian cells. Mammalian expression systems are also known in the art, and include retroviral and adenoviral systems. One expression vector system is a retroviral vector system such as is generally described in PCT/US97/01019 and PCT/US97/01048, both of which are hereby expressly incorporated by reference. Of particular use as mammalian promoters are the promoters from mammalian viral genes, since the viral genes are often highly expressed and have a broad host range. Examples include the SV40 early promoter, mouse mammary tumor virus LTR promoter, adenovirus major late promoter, herpes simplex virus promoter, and the CMV promoter (see, e.g., Fernandez and Hoeffler, supra). Typically, transcription termination and polyadenylation sequences recognized by mammalian cells are regulatory regions located 3' to the translation stop codon and thus, together with the promoter elements, flank the coding sequence. Examples of transcription terminator and polyadenylation signals include those derived from SV40.

The methods of introducing exogenous nucleic acid into mammalian hosts, as well as other hosts, is well known in the art, and will vary with the host cell used. Techniques include dextran-mediated transfection, calcium phosphate precipitation, polybrene mediated transfection, protoplast fusion, electroporation, viral infection, encapsulation of the polynucleotide(s) in liposomes, and direct microinjection of the DNA into nuclei.

In a preferred embodiment, prostate cancer proteins are expressed in bacterial systems. Bacterial expression systems are well known in the art. Promoters from bacteriophage may also be used and are known in the art. In addition, synthetic promoters and hybrid promoters are also useful; e.g., the tac promoter is a hybrid of the trp and lac promoter sequences. Furthermore, a bacterial promoter can include naturally occurring promoters of non-bacterial origin that have the ability to bind bacterial RNA polymerase and initiate transcription. In addition to a functioning promoter sequence, an efficient ribosome

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binding site is desirable. The expression vector may also include a signal peptide sequence that provides for secretion of the prostate cancer protein in bacteria. The protein is either secreted into the growth media (gram-positive bacteria) or into the periplasmic space, located between the inner and outer membrane of the cell (gram-negative bacteria). The bacterial expression vector may also include a selectable marker gene to allow for the selection of bacterial strains that have been transformed. Suitable selection genes include genes which render the bacteria resistant to drugs such as ampicillin, chloramphenicol, erythromycin, kanamycin, neomycin and tetracycline. Selectable markers also include biosynthetic genes, such as those in the histidine, tryptophan and leucine biosynthetic pathways. These components are assembled into expression vectors. Expression vectors for bacteria are well known in the art, and include vectors for Bacillus subtilis, E. coli, Streptococcus cremoris, and Streptococcus lividans, among others (e.g., Fernandez and Hoeffler, supra). The bacterial expression vectors are transformed into bacterial host cells using techniques well known in the art, such as calcium chloride treatment, electroporation, and others.

In one embodiment, prostate cancer proteins are produced in insect cells. Expression vectors for the transformation of insect cells, and in particular, baculovirus-based expression vectors, are well known in the art.

In a preferred embodiment, prostate cancer protein is produced in yeast cells. Yeast expression systems are well known in the art, and include expression vectors for Saccharomyces cerevisiae, Candida albicans and C. maltosa, Hansenula polymorpha, Kluyveromyces fragilis and K. lactis, Pichia guillerimondii and P. pastoris, Schizosaccharomyces pombe, and Yarrowia lipolytica.

The prostate cancer protein may also be made as a fusion protein, using techniques well known in the art. Thus, e.g., for the creation of monoclonal antibodies, if the desired epitope is small, the prostate cancer protein may be fused to a carrier protein to form an immunogen. Alternatively, the prostate cancer protein may be made as a fusion protein to increase expression, or for other reasons. For example, when the prostate cancer protein is a prostate cancer peptide, the nucleic acid encoding the peptide may be linked to other nucleic acid for expression purposes.

In a preferred embodiment, the prostate cancer protein is purified or isolated after expression. Prostate cancer proteins may be isolated or purified in a variety of ways known to those skilled in the art depending on what other components are present in the sample.

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Standard purification methods include electrophoretic, molecular, immunological and chromatographic techniques, including ion exchange, hydrophobic, affinity, and reverse-phase HPLC chromatography, and chromatofocusing. For example, the prostate cancer protein may be purified using a standard anti-prostate cancer protein antibody column.

Ultrafiltration and diafiltration techniques, in conjunction with protein concentration, are also useful. For general guidance in suitable purification techniques, see Scopes (1982) Protein Purification Springer-Verlag. The degree of purification necessary will vary depending on the use of the prostate cancer protein. In some instances no purification will be necessary.

Once expressed and purified if necessary, the prostate cancer proteins and nucleic acids are useful in a number of applications. They may be used as immunoselection reagents, as vaccine reagents, as screening agents, etc.

Variants of prostate cancer proteins

In one embodiment, the prostate cancer proteins are derivative or variant prostate cancer proteins as compared to the wild-type sequence. That is, as outlined more fully below, the derivative prostate cancer peptide will often contain at least one amino acid substitution, deletion or insertion, with amino acid substitutions being particularly preferred. The amino acid substitution, insertion, or deletion may occur at most any residue within the prostate cancer peptide.

Also included within one embodiment of prostate cancer proteins of the present invention are amino acid sequence variants. These variants typically fall into one or more of three classes: substitutional, insertional, or deletional variants. These variants ordinarily are prepared by site specific mutagenesis of nucleotides in the DNA encoding the prostate cancer protein, using cassette or PCR mutagenesis or other techniques well known in the art, to produce DNA encoding the variant, and thereafter expressing the DNA in recombinant cell culture as outlined above. However, variant prostate cancer protein fragments having up to about 100-150 residues may be prepared by in vitro synthesis using established techniques. Amino acid sequence variants are characterized by the predetermined nature of the variation, a feature that sets them apart from naturally occurring allelic or interspecies variation of the prostate cancer protein amino acid sequence. The variants typically exhibit the same qualitative biological activity as the naturally occurring analogue, although variants can also be selected which have modified characteristics as will be more fully outlined below.

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While the site or region for introducing an amino acid sequence variation is predetermined, the mutation per se need not be predetermined. For example, in order to optimize the performance of a mutation at a given site, random mutagenesis may be conducted at the target codon or region and the expressed prostate cancer variants screened for the optimal combination of desired activity. Techniques for making substitution mutations at predetermined sites in DNA having a known sequence are well known, e.g., M13 primer mutagenesis and PCR mutagenesis. Screening of the mutants is done using assays of prostate cancer protein activities.

Amino acid substitutions are typically of single residues; insertions usually will be on the order of from about 1 to 20 amino acids, although considerably larger insertions may be tolerated. Deletions range from about 1 to about 20 residues, although in some cases deletions may be much larger.

Substitutions, deletions, insertions or a combination thereof may be used to arrive at a final derivative. Generally these changes are done on a few amino acids to minimize the alteration of the molecule. However, larger changes may be tolerated in certain circumstances. When small alterations in the characteristics of the prostate cancer protein are desired, substitutions are generally made in accordance with the amino acid substitution relationships provided in the definition section.

The variants typically exhibit the same qualitative biological activity and will elicit the same immune response as the naturally-occurring analog, although variants also are selected to modify the characteristics of the prostate cancer proteins as needed. Alternatively, the variant may be designed such that the biological activity of the prostate cancer protein is altered. For example, glycosylation sites may be altered or removed.

Substantial changes in function or immunological identity are made by selecting substitutions that are less conservative than those described above. For example, substitutions may be made which more significantly affect: the structure of the polypeptide backbone in the area of the alteration, for example the alpha-helical or beta-sheet structure; the charge or hydrophobicity of the molecule at the target site; or the bulk of the side chain. The substitutions which in general are expected to produce the greatest changes in the polypeptide's properties are those in which (a) a hydrophilic residue, e.g., serinyl or threonyl is substituted for (or by) a hydrophobic residue, e.g., leucyl, isoleucyl, phenylalanyl, valyl or alanyl; (b) a cysteine or proline is substituted for (or by) another residue; (c) a residue having

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an electropositive side chain, e.g., lysyl, arginyl, or histidyl, is substituted for (or by) an electronegative residue, e.g., glutamyl or aspartyl; or (d) a residue having a bulky side chain, e.g., phenylalanine, is substituted for (or by) one not having a side chain, e.g., glycine.

Covalent modifications of prostate cancer polypeptides are included within the scope of this invention. One type of covalent modification includes reacting targeted amino acid residues of a prostate cancer polypeptide with an organic derivatizing agent that is capable of reacting with selected side chains or the N-or C-terminal residues of a prostate cancer polypeptide. Derivatization with bifunctional agents is useful, for instance, for crosslinking prostate cancer polypeptides to a water-insoluble support matrix or surface for use in the method for purifying anti-prostate cancer polypeptide antibodies or screening assays, as is more fully described below. Commonly used crosslinking agents include, e.g., 1,1-bis(diazoacetyl)-2-phenylethane, glutaraldehyde, N-hydroxysuccinimide esters, e.g., esters with 4-azidosalicylic acid, homobifunctional imidoesters, including disuccinimidyl esters such as 3,3'-dithiobis(succinimidylpropionate), bifunctional maleimides such as bis-N-maleimido-1,8-octane and agents such as methyl-3-((p-azidophenyl)dithio)propionimidate.

Other modifications include deamidation of glutaminyl and asparaginyl residues to the corresponding glutamyl and aspartyl residues, respectively, hydroxylation of proline and lysine, phosphorylation of hydroxyl groups of serinyl, threonyl or tyrosyl residues, methylation of the amino groups of the lysine, arginine, and histidine side chains (e.g., pp. 79-86, Creighton (1983) <u>Proteins: Structure and Molecular Properties</u> Freeman), acetylation of the N-terminal amine, and amidation of a C-terminal carboxyl group.

Another type of covalent modification of the prostate cancer polypeptide included within the scope of this invention comprises altering the native glycosylation pattern of the polypeptide. "Altering the native glycosylation pattern" is intended for purposes herein to mean deleting one or more carbohydrate moieties found in native sequence prostate cancer polypeptide, and/or adding one or more glycosylation sites that are not present in the native sequence prostate cancer polypeptide. Glycosylation patterns can be altered in many ways. For example the use of different cell types to express prostate cancer-associated sequences can result in different glycosylation patterns.

Addition of glycosylation sites to prostate cancer polypeptides may also be accomplished by altering the amino acid sequence thereof. The alteration may be made, e.g., by the addition of, or substitution by, one or more serine or threonine residues to the native

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sequence prostate cancer polypeptide (for O-linked glycosylation sites). The prostate cancer amino acid sequence may optionally be altered through changes at the DNA level, particularly by mutating the DNA encoding the prostate cancer polypeptide at preselected bases such that codons are generated that will translate into the desired amino acids.

Another means of increasing the number of carbohydrate moieties on the prostate cancer polypeptide is by chemical or enzymatic coupling of glycosides to the polypeptide. Such methods are described in the art, e.g., in WO 87/05330, and pp. 259-306 in Aplin and Wriston (1981) CRC Crit. Rev. Biochem.

Removal of carbohydrate moieties present on the prostate cancer polypeptide may be accomplished chemically or enzymatically or by mutational substitution of codons encoding for amino acid residues that serve as targets for glycosylation. Chemical deglycosylation techniques are known in the art and described, e.g., by Hakimuddin, et al. (1987) <u>Arch. Biochem. Biophys.</u> 259:52-57; and Edge, et al. (1981) <u>Anal. Biochem.</u> 118:131-137.

Enzymatic cleavage of carbohydrate moieties on polypeptides can be achieved by the use of a variety of endo-and exo-glycosidases as described by Thotakura, et al. (1987) <u>Meth.</u>
Enzymal. 138:350-359.

Another type of covalent modification of prostate cancer comprises linking the prostate cancer polypeptide to one of a variety of nonproteinaceous polymers, e.g., polyethylene glycol, polypropylene glycol, or polyoxyalkylenes, in the manner set forth in U.S. Patent Nos. 4,640,835; 4,496,689; 4,301,144; 4,670,417; 4,791,192; or 4,179,337.

Prostate cancer polypeptides of the present invention may also be modified in a way to form chimeric molecules comprising a prostate cancer polypeptide fused to another, heterologous polypeptide or amino acid sequence. In one embodiment, such a chimeric molecule comprises a fusion of a prostate cancer polypeptide with a tag polypeptide which provides an epitope to which an anti-tag antibody can selectively bind. The epitope tag is generally placed at the amino-or carboxyl-terminus of the prostate cancer polypeptide. The presence of such epitope-tagged forms of a prostate cancer polypeptide can be detected using an antibody against the tag polypeptide. Also, provision of the epitope tag enables the prostate cancer polypeptide to be readily purified by affinity purification using an anti-tag antibody or another type of affinity matrix that binds to the epitope tag. In an alternative embodiment, the chimeric molecule may comprise a fusion of a prostate cancer polypeptide

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with an immunoglobulin or a particular region of an immunoglobulin. For a bivalent form of the chimeric molecule, such a fusion could be to the Fc region of an IgG molecule.

Various tag polypeptides and their respective antibodies are well known in the art. Examples include poly-histidine (poly-his) or poly-histidine-glycine (poly-his-gly) tags; HIS6 and metal chelation tags, the flu HA tag polypeptide and its antibody 12CA5 (Field, et al. (1988) Mol. Cell. Biol. 8:2159-2165; the e-myc tag and the 8F9, 3C7, 6E10, G4, B7, and 9E10 antibodies thereto (Evan, et al. (1985) Molecular and Cellular Biology 5:3610-3616); and the Herpes Simplex virus glycoprotein D (gD) tag and its antibody (Paborsky, et al. (1990) Protein Engineering 3:547-553). Other tag polypeptides include the Flag-peptide (Hopp, et al. (1988) BioTechnology 6:1204-1210); the KT3 epitope peptide (Martin, et al. (1992) Science 255:192-194); tubulin epitope peptide (Skinner, et al. (1991) J. Biol. Chem. 266:15163-15166); and the T7 gene 10 protein peptide tag (Lutz-Freyermuth, et al. (1990) Proc. Natl. Acad. Sci. USA 87:6393-6397).

Also included are other prostate cancer proteins of the prostate cancer family, and prostate cancer proteins from other organisms, which are cloned and expressed as outlined below. Thus, probe or degenerate polymerase chain reaction (PCR) primer sequences may be used to find other related prostate cancer proteins from humans or other organisms. As will be appreciated by those in the art, particularly useful probe and/or PCR primer sequences include the unique areas of the prostate cancer nucleic acid sequence. As is generally known in the art, preferred PCR primers are from about 15 to about 35 nucleotides in length, with from about 20 to about 30 being preferred, and may contain inosine as needed. The conditions for the PCR reaction are well known in the art (e.g., Innis, PCR Protocols, supra).

Antibodies to prostate cancer proteins

In a preferred embodiment, when the prostate cancer protein is to be used to generate antibodies, e.g., for immunotherapy or immunodiagnosis, the prostate cancer protein should share at least one epitope or determinant with the full length protein. By "epitope" or "determinant" herein is typically meant a portion of a protein which will generate and/or bind an antibody or T-cell receptor in the context of MHC. Thus, in most instances, antibodies made to a smaller prostate cancer protein will be able to bind to the full-length protein, particularly linear epitopes. In a preferred embodiment, the epitope is unique; that is, antibodies generated to a unique epitope show little or no cross-reactivity.

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Methods of preparing polyclonal antibodies are known to the skilled artisan (e.g., Coligan, supra; and Harlow and Lane, supra). Polyclonal antibodies can be raised in a mammal, e.g., by one or more injections of an immunizing agent and, if desired, an adjuvant. Typically, the immunizing agent and/or adjuvant will be injected in the mammal by multiple subcutaneous or intraperitoneal injections. The immunizing agent may include a protein encoded by a nucleic acid of the figures or fragment thereof or a fusion protein thereof. It may be useful to conjugate the immunizing agent to a protein known to be immunogenic in the mammal being immunized. Examples of such immunogenic proteins include but are not limited to keyhole limpet hemocyanin, serum albumin, bovine thyroglobulin, and soybean trypsin inhibitor. Examples of adjuvants which may be employed include Freund's complete adjuvant and MPL-TDM adjuvant (monophosphoryl Lipid A, synthetic trehalose dicorynomycolate). The immunization protocol may be selected by one skilled in the art without undue experimentation.

The antibodies may, alternatively, be monoclonal antibodies. Monoclonal antibodies may be prepared using hybridoma methods, such as those described by Kohler and Milstein (1975) Nature 256:495. In a hybridoma method, a mouse, hamster, or other appropriate host animal, is typically immunized with an immunizing agent to elicit lymphocytes that produce or are capable of producing antibodies that will specifically bind to the immunizing agent. Alternatively, the lymphocytes may be immunized in vitro. The immunizing agent will typically include a polypeptide encoded by a nucleic acid of Tables 1A-4 or fragment thereof, or a fusion protein thereof. Generally, either peripheral blood lymphocytes ("PBLs") are used if cells of human origin are desired, or spleen cells or lymph node cells are used if nonhuman mammalian sources are desired. The lymphocytes are then fused with an immortalized cell line using a suitable fusing agent, such as polyethylene glycol, to form a hybridoma cell (see pp. 59-103 in Goding (1986) Monoclonal Antibodies: Principles and Practice Academic Press). Immortalized cell lines are usually transformed mammalian cells, particularly myeloma cells of rodent, bovine and human origin. Usually, rat or mouse myeloma cell lines are employed. The hybridoma cells may be cultured in a suitable culture medium that preferably contains one or more substances that inhibit the growth or survival of the unfused, immortalized cells. For example, if the parental cells lack the enzyme hypoxanthine guanine phosphoribosyl transferase (HGPRT or HPRT), the culture medium

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for the hybridomas typically will include hypoxanthine, aminopterin, and thymidine ("HAT medium"), which substances prevent the growth of HGPRT-deficient cells.

In one embodiment, the antibodies are bispecific antibodies. Bispecific antibodies are monoclonal, preferably human or humanized, antibodies that have binding specificities for at least two different antigens or that have binding specificities for two epitopes on the same antigen. In one embodiment, one of the binding specificities is for a protein encoded by a nucleic acid of Tables 1A-4 or a fragment thereof, the other one is for another antigen, and preferably for a cell-surface protein or receptor or receptor subunit, preferably one that is tumor specific. Alternatively, tetramer-type technology may create multivalent reagents.

In a preferred embodiment, the antibodies to prostate cancer protein are capable of reducing or eliminating a biological function of a prostate cancer protein, as is described below. That is, the addition of anti-prostate cancer protein antibodies (either polyclonal or preferably monoclonal) to prostate cancer tissue (or cells containing prostate cancer) may reduce or eliminate the prostate cancer. Generally, at least a 25% decrease in activity, growth, size or the like is preferred, with at least about 50% being particularly preferred and about a 95-100% decrease being especially preferred.

In a preferred embodiment the antibodies to the prostate cancer proteins are humanized antibodies (e.g., Xenerex Biosciences; Medarex, Inc.; Abgenix, Inc.; Protein Design Labs, Inc.). Humanized forms of non-human (e.g., murine) antibodies are chimeric molecules of immunoglobulins, immunoglobulin chains or fragments thereof (such as Fv. Fab. Fab', F(ab')2 or other antigen-binding subsequences of antibodies) which contain minimal sequence derived from non-human immunoglobulin. Humanized antibodies include human immunoglobulins (recipient antibody) in which residues from a complementary determining region (CDR) of the recipient are replaced by residues from a CDR of a nonhuman species (donor antibody) such as mouse, rat or rabbit having the desired specificity, affinity and capacity. In some instances, Fv framework residues of the human immunoglobulin are replaced by corresponding non-human residues. Humanized antibodies may also comprise residues which are found neither in the recipient antibody nor in the imported CDR or framework sequences. In general, a humanized antibody will comprise substantially all of at least one, and typically two, variable domains, in which all or substantially all of the CDR regions correspond to those of a non-human immunoglobulin and all or substantially all of the framework (FR) regions are those of a human

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immunoglobulin consensus sequence. The humanized antibody optimally also will comprise at least a portion of an immunoglobulin constant region (Fc), typically that of a human immunoglobulin (Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 332:323-329; and Presta (1992) Curr. Op. Struct. Biol. 2:593-596). Humanization can be essentially performed following methods of Winter and co-workers (see, e.g., Jones, et al. (1986) Nature 321:522-525; Riechmann, et al. (1988) Nature 322:323-327; and Verhoeyen, et al. (1988) Science 239:1534-1536), by substituting rodent CDRs or CDR sequences for the corresponding sequences of a human antibody. Accordingly, such humanized antibodies are chimeric antibodies (U.S. Patent No. 4,816,567), wherein substantially less than an intact human variable domain has been substituted by the corresponding sequence from a non-human species.

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Human antibodies can also be produced using various techniques known in the art, including phage display libraries (Hoogenboom and Winter (1991) J. Mol. Biol. 227:381-388; Marks, et al. (1991) J. Mol. Biol. 222:581-597) or the preparation of human monoclonal antibodies (e.g., p77 in Cole, et al. (1985) Monoclonal Antibodies and Cancer Therapy Liss; and Boerner, et al. (1991) J. Immunol. 147(1):86-95). Similarly, human antibodies can be made by introducing of human immunoglobulin loci into transgenic animals, e.g., mice in which the endogenous immunoglobulin genes have been partially or completely inactivated. Upon challenge, human antibody production is observed, which closely resembles that seen in humans in most respects, including gene rearrangement, assembly, and antibody repertoire. This approach is described, e.g., in U.S. Patent Nos. 5,545,807; 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,661,016, and in the following scientific publications: Marks, et al. (1992) Bio/Technology 10:779-783; Lonberg, et al. (1994) Nature 368:812-13; Fishwild, et al. (1996) Nature Biotechnology 14:845-51; Neuberger (1996) Nature Biotechnology 14:826; Lonberg and Huszar (1995) Intern. Rev. Immunol. 13:65-93.

By immunotherapy is meant treatment of prostate cancer with an antibody raised against prostate cancer proteins. As used herein, immunotherapy can be passive or active. Passive immunotherapy as defined herein is the passive transfer of antibody to a recipient (patient). Active immunization is the induction of antibody and/or T-cell responses in a recipient (patient). Induction of an immune response is the result of providing the recipient with an antigen to which antibodies are raised. As appreciated by one of ordinary skill in the

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art, the antigen may be provided by injecting a polypeptide against which antibodies are desired to be raised into a recipient, or contacting the recipient with a nucleic acid capable of expressing the antigen and under conditions for expression of the antigen, leading to an immune response.

In a preferred embodiment the prostate cancer proteins against which antibodies are raised are secreted proteins as described above. Without being bound by theory, antibodies used for treatment, bind and prevent the secreted protein from binding to its receptor, thereby inactivating the secreted prostate cancer protein.

In another preferred embodiment, the prostate cancer protein to which antibodies are raised is a transmembrane protein. Without being bound by theory, antibodies used for treatment bind the extracellular domain of the prostate cancer protein and prevent it from binding to other proteins, such as circulating ligands or cell-associated molecules. The antibody may cause down-regulation of the transmembrane prostate cancer protein. As will be appreciated by one of ordinary skill in the art, the antibody may be a competitive, noncompetitive or uncompetitive inhibitor of protein binding to the extracellular domain of the prostate cancer protein. The antibody is also often an antagonist of the prostate cancer protein. Further, the antibody may prevent activation of the transmembrane prostate cancer protein. In one aspect, when the antibody prevents the binding of other molecules to the prostate cancer protein, the antibody prevents growth of the cell. The antibody may also be used to target or sensitize the cell to cytotoxic agents, including, but not limited to TNF-a, TNF-\u03b3, IL-1, INF-\u03b3, and IL-2, or chemotherapeutic agents including 5FU, vinblastine, actinomycin D, cisplatin, methotrexate, and the like. In some instances the antibody belongs to a sub-type that activates serum complement when complexed with the transmembrane protein thereby mediating cytotoxicity or antigen-dependent cytotoxicity (ADCC). Thus, prostate cancer is treated by administering to a patient antibodies directed against the transmembrane prostate cancer protein. Antibody-labeling may activate a co-toxin, localize a toxin payload, or otherwise provide means to locally ablate cells.

In another preferred embodiment, the antibody is conjugated to an effector moiety.

The effector moiety can be a labeling moiety such as a radioactive label or fluorescent label, or can be a therapeutic moiety. In one aspect the therapeutic moiety is a small molecule that modulates the activity of the prostate cancer protein. In another aspect the therapeutic moiety modulates the activity of molecules associated with or in close proximity to the prostate

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cancer protein. The therapeutic moiety may inhibit enzymatic activity such as protease or collagenase or protein kinase activity associated with prostate cancer.

In a preferred embodiment, the therapeutic moiety can also be a cytotoxic agent. In this method, targeting the cytotoxic agent to prostate cancer tissue or cells, results in a reduction in the number of afflicted cells, thereby reducing symptoms associated with prostate cancer. Cytotoxic agents are numerous and varied and include, but are not limited to, cytotoxic drugs or toxins or active fragments of such toxins. Suitable toxins and their corresponding fragments include diphtheria A chain, exotoxin A chain, ricin A chain, abrin A chain, curcin, crotin, phenomycin, enomycin, saporin, auristatin, and the like. Cytotoxic agents also include radiochemicals made by conjugating radioisotopes to antibodies raised against prostate cancer proteins, or binding of a radionuclide to a chelating agent that has been covalently attached to the antibody. Targeting the therapeutic moiety to transmembrane prostate cancer proteins not only serves to increase the local concentration of therapeutic moiety in the prostate cancer afflicted area, but also serves to reduce deleterious side effects, e.g., by binding to normal tissues, that may be associated with the therapeutic moiety.

In another preferred embodiment, the prostate cancer protein against which the antibodies are raised is an intracellular protein. In this case, the antibody may be conjugated to a protein which facilitates entry into the cell. In one case, the antibody enters the cell by endocytosis. In another embodiment, a nucleic acid encoding the antibody is administered to the individual or cell. Moreover, wherein the prostate cancer protein can be targeted within a cell, i.e., the nucleus, an antibody thereto contains a signal for that target localization, i.e., a nuclear localization signal.

The prostate cancer antibodies of the invention specifically bind to prostate cancer proteins. By "specifically bind" herein is meant that the antibodies bind to the protein with a K_d of at least about 0.1 mM, more usually at least about 1 μM , preferably at least about 0.1 μM or better, and most preferably, 0.01 μM or better. Selectivity of binding is also important.

Detection of prostate cancer sequence for diagnostic and therapeutic applications

In one aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell

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division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in 1A). Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A). Still other genes are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-hi-hi pattern in Table 1A). Thus, the data suggest that different antigens are expressed in quiescent cells and actively dividing androgen-independent prostate cancer cells.

In another aspect, the RNA expression levels of genes are determined for different cellular states in the prostate cancer phenotype. After androgen ablation therapy, cells that survive the therapy undergo a period of quiescence followed at sometime later by active cell division. As explained above, there are a variety of expression patterns characteristic of the prostate cancer genes involved in androgen-independent prostate cancer. Some genes are expressed early in the time course following ablation therapy, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A). Other genes are expressed early in the time course following ablation therapy, then drop off in expression, and do not express again with emergence of androgenindependence (hi-lo-lo-lo and hi-hi-lo-lo pattern in Table 2A). Still other genes are not expressed early in the time course, but express only with emergence of androgenindependence (lo-lo-lo-hi pattern in Table 2A). Other genes are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A). Finally, some genes are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A). Thus, the data suggest that different antigens are expressed in quiescent cells (during androgen withdrawal) and actively dividing androgen-independent prostate cancer cells.

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Effective therapy to combat androgen-independent prostate cancer requires that the timing of therapy coincide with expression of the target genes. Patients can be monitored for the expression of certain diagnostic antigens that indicate the presence of quiescent cells or which indicate the transition to actively dividing androgen-independent prostate cancer cells. Thus, therapy to combat androgen-independent prostate cancer should begin at some time following androgen ablation therapy, depending on the particular target. Typically the transition from quiescence to actively dividing androgen-independent prostate cancer occurs between 6-24 months following androgen ablation therapy. Thus, preferred time periods for the therapies of the invention are as follows:

Expression levels of genes in normal tissue (i.e., not undergoing prostate cancer) and in prostate cancer tissue (and in some cases, for varying severities of prostate cancer that relate to prognosis, as outlined below) or in non-malignant disease are evaluated to provide expression profiles. An expression profile of a particular cell state or point of development is essentially a "fingerprint" of the state. While two states may have a particular gene similarly expressed, the evaluation of a number of genes simultaneously allows the generation of a gene expression profile that is reflective of the state of the cell. By comparing expression profiles of cells in different states, information regarding which genes are important (including both up- and down-regulation of genes) in each of these states is obtained. Then, diagnosis may be performed or confirmed to determine whether a tissue sample has the gene expression profile of normal or cancerous tissue. This will provide for molecular diagnosis of related conditions.

"Differential expression," or grammatical equivalents as used herein, refers to qualitative or quantitative differences in the temporal and/or cellular gene expression patterns within and among cells and tissue. Thus, a differentially expressed gene can qualitatively have its expression altered, including an activation or inactivation, in, e.g., normal versus prostate cancer tissue. Genes may be turned on or turned off in a particular state, relative to another state thus permitting comparison of two or more states. A qualitatively regulated gene will exhibit an expression pattern within a state or cell type which is detectable by standard techniques. Some genes will be expressed in one state or cell type, but not in both. Alternatively, the difference in expression may be quantitative, e.g., in that expression is increased or decreased; i.e., gene expression is either upregulated, resulting in an increased amount of transcript. The

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degree to which expression differs need only be large enough to quantify via standard characterization techniques as outlined below, such as by use of Affymetrix GeneChip™ expression arrays, Lockhart (1996) Nature Biotechnology 14:1675-1680, hereby expressly incorporated by reference. Other techniques include, but are not limited to, quantitative reverse transcriptase PCR, northern analysis and RNase protection. As outlined above, preferably the change in expression (i.e., upregulation or downregulation) is at least about 50%, more preferably at least about 100%, more preferably at least about 200%, with from 300 to at least 1000% being especially preferred.

Evaluation may be at the gene transcript, or the protein level. The amount of gene expression may be monitored using nucleic acid probes to the DNA or RNA equivalent of the gene transcript, and the quantification of gene expression levels, or, alternatively, the final gene product itself (protein) can be monitored, e.g., with antibodies to the prostate cancer protein and standard immunoassays (ELISAs, etc.) or other techniques, including mass spectroscopy assays, 2D gel electrophoresis assays, etc. Proteins corresponding to prostate cancer genes, i.e., those identified as being important in a prostate cancer or disease phenotype, can be evaluated in a prostate cancer diagnostic test.

In a preferred embodiment, gene expression monitoring is performed simultaneously on a number of genes. Multiple protein expression monitoring can be performed as well.

Similarly, these assays may be performed on an individual basis as well.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a particular cell. The assays are further described below in the example. PCR techniques can be used to provide greater sensitivity.

In a preferred embodiment nucleic acids encoding the prostate cancer protein are detected. Although DNA or RNA encoding the prostate cancer protein may be detected, of particular interest are methods wherein an mRNA encoding a prostate cancer protein is detected. Probes to detect mRNA can be a nucleotide/deoxynucleotide probe that is complementary to and hybridizes with the mRNA and includes, but is not limited to, oligonucleotides, cDNA, or RNA. Probes also should contain a detectable label, as defined herein. In one method the mRNA is detected after immobilizing the nucleic acid to be examined on a solid support such as nylon membranes and hybridizing the probe with the sample. Following washing to remove the non-specifically bound probe, the label is

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detected. In another method detection of the mRNA is performed in situ (in situ hybridization or ISH). In this method permeabilized cells or tissue samples are contacted with a detectably labeled nucleic acid probe for sufficient time to allow the probe to hybridize with the target mRNA. Following washing to remove the non-specifically bound probe, the label is detected. For example a digoxygenin labeled riboprobe (RNA probe) that is complementary to the mRNA encoding a prostate cancer protein is detected by binding the digoxygenin with an anti-digoxygenin secondary antibody and developed with nitro blue tetrazolium and 5-bromo-4-chloro-3-indoyl phosphate.

In a preferred embodiment, various proteins from the three classes of proteins as described herein (secreted, transmembrane, or intracellular proteins) are used in diagnostic assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins and cells containing prostate cancer sequences are used in diagnostic assays. Such may evaluate tissues, e.g., immunohistochemistry, or evaluate body fluids, e.g., blood. The detection may be direct of cells, or indirect, e.g., of products from cells. This can be performed on an individual gene or corresponding polypeptide level. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes and/or corresponding polypeptides.

As described and defined herein, prostate cancer proteins, including intracellular, transmembrane, or secreted proteins, find use as prognostic or diagnostic markers of prostate cancer or other prostate conditions. Detection of these proteins in putative prostate cancer tissue allows for detection, diagnosis, or prognosis of prostate proliferative disorders (malignant and non-malignant) including benign prostate hyperplasia (BPH) and cancer, and prostatitis. Diagnosis may also assist in selecting a therapeutic strategy, e.g., based on expression profiles and/or comparison to archival samples. In one embodiment, antibodies are used to detect prostate cancer proteins, directly or indirectly. A preferred method separates proteins from a sample by electrophoresis on a gel (typically a denaturing and reducing protein gel, but may be another type of gel, including isoelectric focusing gels and the like). Following separation of proteins, the prostate cancer protein is detected, e.g., by immunoblotting with antibodies raised against the prostate cancer protein. Methods of immunoblotting are well known to those of ordinary skill in the art.

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In another preferred method, antibodies to the prostate cancer protein find use in in situ imaging techniques, e.g., in histology and/or in immunohistochemistry (e.g., Asai (ed. 1993) Methods in Cell Biology: Antibodies in Cell Biology (vol. 37) Academic Press. In this method cells are contacted with from one to many antibodies to the prostate cancer protein(s). Following washing to remove non-specific antibody binding, the presence of the antibody or antibodies is detected. In one embodiment the antibody is detected by incubating with a secondary antibody that contains a detectable label. In another method the primary antibody to the prostate cancer protein(s) contains a detectable label, e.g., an enzyme marker that can act on a substrate. In another preferred embodiment each one of multiple primary antibodies contains a distinct and detectable label. This method finds particular use in simultaneous screening for a plurality of prostate cancer proteins. As will be appreciated by one of ordinary skill in the art, many other histological imaging techniques are also provided by the invention.

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In a preferred embodiment the label is detected in a fluorometer which has the ability to detect and distinguish emissions of different wavelengths. In addition, a fluorescence activated cell sorter (FACS) can be used in the method.

In another preferred embodiment, antibodies find use in diagnosing prostate cancer from blood, serum, plasma, stool, and other samples. Such samples, therefore, are useful as samples to be probed or tested for the presence of prostate cancer proteins, which may be diagnostic of prostate conditions beyond cancer, e.g., BPH. Antibodies can be used to detect a prostate cancer protein by previously described immunoassay techniques including ELISA, immunoblotting (western blotting), immunoprecipitation, BIACORE technology, and the like. Conversely, the presence of antibodies may indicate an immune response against an endogenous prostate cancer protein.

In a preferred embodiment, in situ hybridization of labeled prostate cancer nucleic acid probes to tissue arrays is done. For example, arrays of tissue samples, including prostate cancer tissue and/or normal tissue, are made. In situ hybridization (see, e.g., Ausubel, supra) is then performed. When comparing the fingerprints between an individual and a standard, the skilled artisan can make a diagnosis, a prognosis, or a prediction based on the findings. It is further understood that the genes which indicate the diagnosis may differ from those which indicate the prognosis and molecular profiling of the condition of the cells may lead to distinctions between responsive or refractory conditions or may be predictive of outcomes.

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In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in prognosis assays. As above, gene expression profiles can be generated that correlate to prostate cancer or other prostate disorders, in terms of useful aspects of clinical condition, pathology, or other information which may be relevant to long term prognosis. Again, this may be done on either a protein or gene level, with the use of genes being preferred. Single or multiple genes may be useful in various combinations. As above, prostate cancer probes may be attached to biochips for the detection and quantification of prostate cancer sequences in a tissue or patient. The assays proceed as outlined above for diagnosis. PCR method may provide more sensitive and accurate quantification.

Assays for therapeutic compounds

In a preferred embodiment members of the proteins, nucleic acids, and antibodies as described herein are used in drug screening assays. The prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing prostate cancer sequences are used in drug screening assays or by evaluating the effect of drug candidates on a "gene expression profile" or expression profile of polypeptides. In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent (e.g., Zlokarnik, et al. (1998) Science 279:84-88: Heid (1990) Genome Res. 6:986-94).

In a preferred embodiment, the prostate cancer proteins, antibodies, nucleic acids, modified proteins, and cells containing the native or modified prostate cancer proteins are used in screening assays. That is, the present invention provides novel methods for screening for compositions which modulate the prostate cancer phenotype or an identified physiological function of a prostate cancer protein. As above, this can be done on an individual gene level or by evaluating the effect of drug candidates on a "gene expression profile". In a preferred embodiment, the expression profiles are used, preferably in conjunction with high throughput screening techniques to allow monitoring for expression profile genes after treatment with a candidate agent, see Zlokarnik, supra.

Having identified the differentially expressed genes herein, a variety of assays may be executed. In a preferred embodiment, assays may be run on an individual gene or protein level. That is, having identified a particular gene as up regulated in prostate cancer, test

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compounds can be screened for the ability to modulate gene expression or for binding to the prostate cancer protein. "Modulation" thus includes both an increase and a decrease in gene expression. The preferred amount of modulation will depend on the original change of the gene expression in normal yersus tissue undergoing prostate cancer, with changes of at least 10%, preferably 50%, more preferably 100-300%, and in some embodiments 300-1000% or greater. Thus, if a gene exhibits a 4-fold increase in prostate cancer tissue compared to normal tissue, a decrease of about four-fold is often desired; similarly, a 10-fold decrease in prostate cancer tissue compared to normal tissue often provides a target value of a 10-fold increase in expression to be induced by the test compound.

The amount of gene expression may be monitored using nucleic acid probes and the quantification of gene expression levels, or, alternatively, the gene product itself can be monitored, e.g., through the use of antibodies to the prostate cancer protein and standard immunoassays. Proteomics and separation techniques may also allow quantification of expression.

In a preferred embodiment, gene expression or protein monitoring of a number of entities, i.e., an expression profile, is monitored simultaneously. Such profiles will typically involve a plurality of those entities described herein.

In this embodiment, the prostate cancer nucleic acid probes are attached to biochips as outlined herein for the detection and quantification of prostate cancer sequences in a particular cell. Alternatively, PCR may be used. Thus, a series, e.g., of microtiter plate, may be used with dispensed primers in desired wells. A PCR reaction can then be performed and analyzed for each well.

Expression monitoring can be performed to identify compounds that modify the expression of one or more prostate cancer-associated sequences, e.g., a polynucleotide sequence set out in Tables 1A-4. Generally, in a preferred embodiment, a test modulator is added to the cells prior to analysis. Moreover, screens are also provided to identify agents that modulate prostate cancer, modulate prostate cancer proteins, bind to a prostate cancer protein, or interfere with the binding of a prostate cancer protein and an antibody or other binding partner.

The term "test compound" or "drug candidate" or "modulator" or grammatical equivalents as used herein describes a molecule, e.g., protein, oligopeptide, small organic molecule, polysaccharide, polymucleotide, etc., to be tested for the capacity to directly or

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indirectly alter the prostate cancer phenotype or the expression of a prostate cancer sequence, e.g., a nucleic acid or protein sequence. In preferred embodiments, modulators alter expression profiles, or expression profile nucleic acids or proteins provided herein. In one embodiment, the modulator suppresses a prostate cancer phenotype, e.g., to a normal or non-malignant tissue fingerprint. In another embodiment, a modulator induced a prostate cancer phenotype. Generally, a plurality of assay mixtures are run in parallel with different agent concentrations to obtain a differential response to the various concentrations. Typically, one of these concentrations serves as a negative control, i.e., at zero concentration or below the level of detection.

Drug candidates encompass numerous chemical classes, though typically they are organic molecules, preferably small organic compounds having a molecular weight of more than 100 and less than about 2,500 daltons. Preferred small molecules are less than 2000, or less than 1500, or less than 1000, or less than 500 D. Candidate agents comprise functional groups necessary for structural interaction with proteins, particularly hydrogen bonding, and typically include at least an amine, carbonyl, hydroxyl or carboxyl group, preferably at least two of the functional chemical groups. The candidate agents often comprise cyclical carbon or heterocyclic structures and/or aromatic or polyaromatic structures substituted with one or more of the above functional groups. Candidate agents are also found among biomolecules including peptides, saccharides, fatty acids, steroids, purines, pyrimidines, derivatives, structural analogs, or combinations thereof. Particularly preferred are peptides.

In one aspect, a modulator will neutralize the effect of a prostate cancer protein. By "neutralize" is meant that activity of a protein is inhibited or blocked and the consequent effect on the cell.

In certain embodiments, combinatorial libraries of potential modulators will be screened for an ability to bind to a prostate cancer polypeptide or to modulate activity. Conventionally, new chemical entities with useful properties are generated by identifying a chemical compound (called a "lead compound") with some desirable property or activity, e.g., inhibiting activity, creating variants of the lead compound, and evaluating the property and activity of those variant compounds. Often, high throughput screening (HTS) methods are employed for such an analysis.

In one preferred embodiment, high throughput screening methods involve providing a library containing a large number of potential therapeutic compounds (candidate WO 02/098358 PCT/US02/17594

compounds). Such "combinatorial chemical libraries" are then screened in one or more assays to identify those library members (particular chemical species or subclasses) that display a desired characteristic activity. The compounds thus identified can serve as conventional "lead compounds" or can themselves be used as potential or actual therapeutics.

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A combinatorial chemical library is a collection of diverse chemical compounds generated by either chemical synthesis or biological synthesis by combining a number of chemical "building blocks" such as reagents. For example, a linear combinatorial chemical library, such as a polypeptide (e.g., mutein) library, is formed by combining a set of chemical building blocks called amino acids in most every possible way for a given compound length (i.e., the number of amino acids in a polypeptide compound). Millions of chemical compounds can be synthesized through such combinatorial mixing of chemical building blocks. Gallon, et al. (1994) J. Med. Chem. 37:1233-1251.

Preparation and screening of combinatorial chemical libraries is well known to those of skill in the art. Such combinatorial chemical libraries include, but are not limited to. 15 peptide libraries (see, e.g., U.S. Patent No. 5,010,175, Furka (1991) Pept. Prot. Res. 37:487-493, Houghton, et al. (1991) Nature, 354:84-88), peptoids (PCT Publication No WO 91/19735), encoded peptides (PCT Publication WO 93/20242), random bio-oligomers (PCT Publication WO 92/00091), benzodiazepines (U.S. Pat. No. 5,288,514), diversomers such as hydantoins, benzodiazepines and dipeptides (Hobbs, et al. (1993) Proc. Nat. Acad. Sci. USA 20 90:6909-6913), vinylogous polypeptides (Hagihara, et al. (1992) J. Amer. Chem. Soc. 114:6568-xxx), nonpeptidal peptidomimetics with a Beta-D-Glucose scaffolding (Hirschmann, et al. (1992) J. Amer. Chem. Soc. 114:9217-9218), analogous organic syntheses of small compound libraries (Chen, et al. (1994) J. Amer. Chem. Soc. 116:2661xxx), oligocarbamates (Cho, et al. (1993) Science 261:1303-1305), and/or peptidyl 25 phosphonates (Campbell, et al. (1994) J. Org, Chem. 59:658-xxx). See, generally, Gordon, et al. (1994) J. Med. Chem. 37:1385-1401), nucleic acid libraries (see, e.g., Stratagene, Corp.). peptide nucleic acid libraries (see, e.g., U.S. Patent 5,539,083), antibody libraries (see, e.g., Vaughn, et al. (1996) Nature Biotechnology 14:309-314, and PCT/US96/10287). carbohydrate libraries (see, e.g., Liang, et al. (1996) Science 274:1520-1522, and U.S. Patent No. 5,593,853), and small organic molecule libraries (see, e.g., benzodiazepines, Baum 30 (1993) C&EN, Jan 18, page 33; isoprenoids, U.S. Patent No. 5,569,588; thiazolidinones and metathiazanones, U.S. Patent No. 5,549,974; pyrrolidines, U.S. Patent Nos. 5,525,735 and

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5,519,134; morpholino compounds, U.S. Patent No. 5,506,337; benzodiazepines, U.S. Patent No. 5,288,514; and the like).

Devices for the preparation of combinatorial libraries are commercially available (see, e.g., 357 MPS, 390 MPS, Advanced Chem Tech, Louisville KY, Symphony, Rainin, Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford,

Woburn, MA, 433A Applied Biosystems, Foster City, CA, 9050 Plus, Millipore, Bedford, MA).

A number of well known robotic systems have also been developed for solution phase chemistries. These systems include automated workstations like the automated synthesis apparatus developed by Takeda Chemical Industries, LTD. (Osaka, Japan) and many robotic systems utilizing robotic arms (Zymate II, Zymark Corporation, Hopkinton, Mass.; Orca, Hewlett-Packard, Palo Alto, Calif.), which mimic the manual synthetic operations performed by a chemist. Many of the above devices are suitable for use with the present invention. The nature and implementation of modifications to these devices (if any) so that they can operate as discussed herein will be apparent to persons skilled in the relevant art. In addition, numerous combinatorial libraries are themselves commercially available (see, e.g., ComGenex, Princeton, N.J., Asinex, Moscow, Ru, Tripos, Inc., St. Louis, MO, ChemStar, Ltd, Moscow, RU, 3D Pharmaceuticals, Exton, PA, Martek Biosciences, Columbia, MD, etc.).

The assays to identify modulators are amenable to high throughput screening.

Preferred assays thus detect enhancement or inhibition of prostate cancer gene transcription, inhibition or enhancement of polypeptide expression, and inhibition or enhancement of polypeptide activity.

High throughput assays for the presence, absence, quantification, or other properties of particular nucleic acids or protein products are well known to those of skill in the art. Similarly, binding assays and reporter gene assays are similarly well known. Thus, e.g., U.S. Patent No. 5,559,410 discloses high throughput screening methods for proteins, U.S. Patent No. 5,585,639 discloses high throughput screening methods for nucleic acid binding (i.e., in arrays), while U.S. Patent Nos. 5,576,220 and 5,541,061 disclose high throughput methods of screening for ligand/antibody binding.

In addition, high throughput screening systems are commercially available (see, e.g., Zymark Corp., Hopkinton, MA; Air Technical Industries, Mentor, OH; Beckman Instruments, Inc., Fullerton, CA; Precision Systems, Inc., Natick, MA, etc.). These systems

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typically automate entire procedures, including sample and reagent pipetting, liquid dispensing, timed incubations, and final readings of the microplate in detector(s) appropriate for the assay. These configurable systems provide high throughput and rapid start up as well as a high degree of flexibility and customization. The manufacturers of such systems provide detailed protocols for various high throughput systems. Thus, e.g., Zymark Corp. provides technical bulletins describing screening systems for detecting the modulation of gene transcription, ligand binding, and the like.

In one embodiment, modulators are proteins, often naturally occurring proteins or fragments of naturally occurring proteins. Thus, e.g., cellular extracts containing proteins, or random or directed digests of proteinaceous cellular extracts, may be used. In this way libraries of proteins may be made for screening in the methods of the invention. Particularly preferred in this embodiment are libraries of bacterial, fungal, viral, and mammalian proteins, with the latter being preferred, and human proteins being especially preferred. Particularly useful test compound will be directed to the class of proteins to which the target belongs, e.g., substrates for enzymes or ligands and receptors.

In a preferred embodiment, modulators are peptides of from about 5 to about 30 amino acids, with from about 5 to about 20 amino acids being preferred, and from about 7 to about 15 being particularly preferred. The peptides may be digests of naturally occurring proteins as is outlined above, random peptides, or "biased" random peptides. By "randomized" or grammatical equivalents herein is meant that each nucleic acid and peptide consists of essentially random nucleotides and amino acids, respectively. Since generally these random peptides (or nucleic acids, discussed below) are chemically synthesized, they may typically incorporate any nucleotide or amino acid at any position. The synthetic process can be designed to generate randomized proteins or nucleic acids, to allow the formation of all or most of the possible combinations over the length of the sequence, thus forming a library of randomized candidate bioactive proteinaceous agents.

In one embodiment, the library is fully randomized, with no sequence preferences or constants at any position. In a preferred embodiment, the library is biased. That is, some positions within the sequence are either held constant, or are selected from a limited number of possibilities. For example, in a preferred embodiment, the nucleotides or amino acid residues are randomized within a defined class, e.g., of hydrophobic amino acids, hydrophilic residues, sterically biased (either small or large) residues, towards the creation of nucleic acid

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binding domains, the creation of cysteines, for cross-linking, prolines for SH-3 domains, serines, threonines, tyrosines, or histidines for phosphorylation sites, etc., or to purines, etc.

Modulators of prostate cancer can also be nucleic acids, as defined above.

As described above generally for proteins, nucleic acid modulating agents may be naturally occurring nucleic acids, random nucleic acids, or "biased" random nucleic acids. For example, digests of prokaryotic or eukaryotic genomes may be used as is outlined above for proteins.

In a preferred embodiment, the candidate compounds are organic chemical moieties, a wide variety of which are available in the literature.

After the candidate agent has been added and the cells allowed to incubate for some period of time, the sample containing a target sequence to be analyzed is added to the biochip. If required, the target sequence is prepared using known techniques. For example, the sample may be treated to lyse the cells, using known lysis buffers, electroporation, etc., with purification and/or amplification such as PCR performed as appropriate. For example, an in vitro transcription with labels covalently attached to the nucleotides is performed. Generally, the nucleic acids are labeled with biotin-FITC or PE, or with cy3 or cy5.

In a preferred embodiment, the target sequence is labeled with, e.g., a fluorescent, a chemiluminescent, a chemical, or a radioactive signal, to provide a means of detecting the target sequence's specific binding to a probe. The label also can be an enzyme, such as, alkaline phosphatase or horseradish peroxidase, which the provided with an appropriate substrate produces a product that can be detected. Alternatively, the label can be a labeled compound or small molecule, such as an enzyme inhibitor, that binds but is not catalyzed or altered by the enzyme. The label also can be a moiety or compound, such as, an epitope tag or biotin which specifically binds to streptavidin. For the example of biotin, the streptavidin is labeled as described above, thereby, providing a detectable signal for the bound target sequence. Unbound labeled streptavidin is typically removed prior to analysis.

As will be appreciated by those in the art, these assays can be direct hybridization assays or can comprise "sandwich assays", which include the use of multiple probes, as is generally outlined in U.S. Patent Nos. 5,681,702, 5,597,909, 5,545,730, 5,594,117, 5,591,584, 5,571,670, 5,580,731, 5,571,670, 5,591,584, 5,624,802, 5,635,352, 5,594,118, 5,359,100, 5,124,246, and 5,681,697, each of which is hereby incorporated by reference. In this embodiment, in general, the target nucleic acid is prepared as outlined above, and then

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added to the biochip comprising a plurality of nucleic acid probes, under conditions that allow the formation of a hybridization complex.

A variety of hybridization conditions may be used in the present invention, including high, moderate, and low stringency conditions as outlined above. The assays are generally run under stringency conditions which allows formation of the label probe hybridization complex only in the presence of target. Stringency can be controlled by altering a step parameter that is a thermodynamic variable, including, but not limited to, temperature, formamide concentration, salt concentration, chaotropic salt concentration pH, organic solvent concentration, etc.

These parameters may also be used to control non-specific binding, as is generally outlined in U.S. Patent No. 5,681,697. Thus it may be desirable to perform certain steps at higher stringency conditions to reduce non-specific binding.

The reactions outlined herein may be accomplished in a variety of ways. Components of the reaction may be added simultaneously, or sequentially, in different orders, with preferred embodiments outlined below. In addition, the reaction may include a variety of other reagents. These include salts, buffers, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal hybridization and detection, and/or reduce non-specific or background interactions. Reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may also be used as appropriate, depending on the sample preparation methods and purity of the target.

The assay data are analyzed to determine the expression levels, and changes in expression levels as between states, of individual genes, forming a gene expression profile.

Screens are performed to identify modulators of the prostate cancer or related phenotype. In one embodiment, screening is performed to identify modulators that can induce or suppress a particular expression profile, thus preferably generating the associated phenotype. In another embodiment, e.g., for diagnostic applications, having identified differentially expressed genes important in a particular state, screens can be performed to identify modulators that alter expression of individual genes. In an another embodiment, screening is performed to identify modulators that alter a biological function of the expression product of a differentially expressed gene. Again, having identified the importance of a gene in a particular state, screens are performed to identify agents that bind and/or modulate the biological activity of the gene product.

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In addition screens can be done for genes that are induced in response to a candidate agent. After identifying a modulator based upon its ability to suppress a prostate cancer expression pattern leading to a normal expression pattern, or to modulate a single prostate cancer gene expression profile so as to mimic the expression of the gene from normal tissue, a screen as described above can be performed to identify genes that are specifically modulated in response to the agent. Comparing expression profiles between normal tissue and agent treated prostate cancer tissue reveals genes that are not expressed in normal tissue or prostate cancer tissue, but are expressed in agent treated tissue. These agent-specific sequences can be identified and used by methods described herein for prostate cancer genes or proteins. In particular these sequences and the proteins they encode find use in marking or identifying agent treated cells. In addition, antibodies can be raised against the agent induced proteins and used to tarest novel therapeutics to the treated prostate cancer tissue sample.

Thus, in one embodiment, a test compound is administered to a population of prostate cancer cells, that have an associated prostate cancer expression profile. By "administration" or "contacting" herein is meant that the candidate agent is added to the cells in such a manner as to allow the agent to act upon the cell, whether by uptake and intracellular action, or by action at the cell surface. In some embodiments, nucleic acid encoding a proteinaceous candidate agent (e.g., a peptide) may be put into a viral construct such as an adenoviral or retroviral construct, and added to the cell, such that expression of the peptide agent is accomplished, e.g., PCT US97/01019. Regulatable gene therapy systems can also be used.

Once the test compound has been administered to the cells, the cells can be washed if desired and are allowed to incubate under preferably physiological conditions for some period of time. The cells are then harvested and a new gene expression profile is generated, as outlined herein.

Thus, e.g., prostate cancer or non-malignant tissue may be screened for agents that modulate, e.g., induce or suppress the prostate cancer or related phenotype. A change in at least one gene, preferably many, of the expression profile indicates that the agent has an effect on prostate cancer activity. By defining such a signature for the prostate cancer phenotype, screens for new drugs that alter the phenotype can be devised. With this approach, the drug target need not be known and need not be represented in the original expression screening platform, nor does the level of transcript for the target protein need to change.

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In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of either the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "prostate cancer proteins" or a "prostate cancer modulatory protein". The prostate cancer modulatory protein may be a fragment, or alternatively, be the full length protein to the fragment encoded by the nucleic acids of the Tables 1A-4. Preferably, the prostate cancer modulatory protein is a fragment. In a preferred embodiment, the prostate cancer amino acid sequence which is used to determine sequence identity or similarity is encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are naturally occurring allelic variants of a protein encoded by a nucleic acid of Tables 1A-4. In another embodiment, the sequences are sequence variants as further described herein.

Preferably, the prostate cancer modulatory protein is a fragment of approximately 14 to 24 amino acids long. More preferably the fragment is a soluble fragment. Preferably, the fragment includes a non-transmembrane region. In a preferred embodiment, the fragment has an N-terminal Cys to aid in solubility. In one embodiment, the C-terminus of the fragment is kept as a free acid and the N-terminus is a free amine to aid in coupling, i.e., to cysteine.

In one embodiment the prostate cancer proteins are conjugated to an immunogenic agent as discussed herein. In one embodiment the prostate cancer protein is conjugated to BSA.

Measurements of prostate cancer polypeptide activity, or of prostate cancer or the prostate cancer phenotype can be performed using a variety of assays. For example, the effects of the test compounds upon the function of the prostate cancer polypeptides can be measured by examining parameters described above. A suitable physiological change that affects activity can be used to assess the influence of a test compound on the polypeptides of this invention. When the functional consequences are determined using intact cells or animals, one can also measure a variety of effects such as, in the case of prostate cancer associated with tumors, tumor growth, tumor metastasis, neovascularization, hormone release, transcriptional changes to both known and uncharacterized genetic markers (e.g., northern blots), changes in cell metabolism such as cell growth or pH changes, and changes

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in intracellular second messengers such as cGMP. In the assays of the invention, a mammalian prostate cancer polypeptide is typically used, e.g., mouse, preferably human.

Assays to identify compounds with modulating activity can be performed in vitro. For example, a prostate cancer polypeptide is first contacted with a potential modulator and 5 incubated for a suitable amount of time, e.g., from 0.5 to 48 hours. In one embodiment, the prostate cancer polypeptide levels are determined in vitro by measuring the level of protein or mRNA. The level of protein is measured using immunoassays such as western blotting, ELISA, and the like with an antibody that selectively binds to the prostate cancer polypeptide or a fragment thereof. For measurement of mRNA, amplification, e.g., using PCR, LCR, or hybridization assays, e.g., northern hybridization, RNAse protection, dot blotting, are preferred. The level of protein or mRNA is detected using directly or indirectly labeled detection agents, e.g., fluorescently or radioactively labeled nucleic acids, radioactively or enzymatically labeled antibodies, and the like, as described herein.

Alternatively, a reporter gene system can be devised using the prostate cancer protein promoter operably linked to a reporter gene such as luciferase, green fluorescent protein, CAT, or \(\beta - gal. \) The reporter construct is typically transfected into a cell. After treatment with a potential modulator, the amount of reporter gene transcription, translation, or activity is measured according to standard techniques known to those of skill in the art.

In a preferred embodiment, as outlined above, screens may be done on individual genes and gene products (proteins). That is, having identified a particular differentially expressed gene as important in a particular state, screening of modulators of the expression of the gene or the gene product itself can be done. The gene products of differentially expressed genes are sometimes referred to herein as "prostate cancer proteins." The prostate cancer protein may be a fragment, or alternatively, be the full length protein corresponding to a fragment shown herein.

In one embodiment, screening for modulators of expression of specific genes is performed. Typically, the expression of only one or a few genes are evaluated. In another embodiment, screens are designed to first find compounds that bind to differentially expressed proteins. These compounds are then evaluated for the ability to modulate differentially expressed activity. Moreover, once initial candidate compounds are identified, variants can be further screened to better evaluate structure activity relationships.

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In a preferred embodiment, binding assays are done. In general, purified or isolated gene product is used; that is, the gene products of one or more differentially expressed nucleic acids are made. For example, antibodies are generated to the protein gene products, and standard immunoassays are run to determine the amount of protein present.

5 Alternatively, cells comprising the prostate cancer proteins can be used in the assays.

Thus, in a preferred embodiment, the methods comprise combining a prostate cancer protein and a candidate compound, and determining the binding of the compound to the prostate cancer protein. Preferred embodiments utilize the human prostate cancer protein, although other mammalian proteins may also be used, e.g., for the development of animal models of human disease. In some embodiments, as outlined herein, variant or derivative prostate cancer proteins may be used.

Generally, in a preferred embodiment of the methods herein, the prostate cancer protein or the candidate agent is non-diffusably bound to an insoluble support having isolated sample receiving areas (e.g., a microtiter plate, an array, etc.). The insoluble supports may be made of a composition to which the compositions can be bound, is readily separated from soluble material, and is otherwise compatible with the overall method of screening. The surface of such supports may be solid or porous and of a convenient shape. Examples of suitable insoluble supports include microtiter plates, arrays, membranes, and beads. These are typically made of glass, plastic (e.g., polystyrene), polysaccharides, nylon or nitrocellulose, teflonTM, etc. Microtiter plates and arrays are especially convenient because a large number of assays can be carried out simultaneously, using small amounts of reagents and samples. The particular manner of binding of the composition should be compatible with the reagents and overall methods of the invention, maintain the activity of the composition. and be nondiffusable. Preferred methods of binding include the use of antibodies (which do not sterically block either the ligand binding site or activation sequence when the protein is bound to the support), direct binding to "sticky" or ionic supports, chemical crosslinking, the synthesis of the protein or agent on the surface, etc. Following binding of the protein or agent, excess unbound material is removed by washing. The sample receiving areas may then be blocked through incubation with bovine serum albumin (BSA), casein, or other innocuous protein or other moiety.

In a preferred embodiment, the prostate cancer protein is bound to the support, and a test compound is added to the assay. Alternatively, the candidate agent is bound to the WO 02/098358 PCT/US02/17594

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support and the prostate cancer protein is added. Novel binding agents include specific antibodies, non-natural binding agents identified in screens of chemical libraries, peptide analogs, etc. Of particular interest are screening assays for agents that have a low toxicity for human cells. A wide variety of assays may be used for this purpose, including labeled in vitro protein-protein binding assays, electrophoretic mobility shift assays, immunoassays for protein binding, functional assays (phosphorylation assays, etc.) and the like.

The determination of the binding of the test modulating compound to the prostate cancer protein may be done in a number of ways. In a preferred embodiment, the compound is labeled, and binding determined directly, e.g., by attaching all or a portion of the prostate cancer protein to a solid support, adding a labeled candidate agent (e.g., a fluorescent label), washing off excess reagent, and determining whether the label is present on the solid support. Various blocking and washing steps may be utilized as appropriate.

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In some embodiments, only one of the components is labeled, e.g., the proteins (or proteinaceous candidate compounds) can be labeled. Alternatively, more than one component can be labeled with different labels, e.g., ¹²⁵I for the proteins and a fluorophor for the compound. Proximity reagents, e.g., quenching or energy transfer reagents are also useful.

In one embodiment, the binding of the test compound is determined by competitive binding assay. The competitor is a binding moiety known to bind to the target molecule (i.e., a prostate cancer protein), such as an antibody, peptide, binding partner, ligand, etc. Under certain circumstances, there may be competitive binding between the compound and the binding moiety, with the binding moiety displacing the compound. In one embodiment, the test compound is labeled. Either the compound, or the competitor, or both, is added first to the protein for a time sufficient to allow binding, if present. Incubations may be performed at a temperature which facilitates optimal activity, typically between 4 and 40° C. Incubation periods are typically optimized, e.g., to facilitate rapid high throughput screening. Typically between 0.1 and 1 hour will be sufficient. Excess reagent is generally removed or washed away. The second component is then added, and the presence or absence of the labeled component is followed, to indicate binding.

In a preferred embodiment, the competitor is added first, followed by the test compound. Displacement of the competitor is an indication that the test compound is binding to the prostate cancer protein and thus is canable of binding to, and potentially modulating,

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the activity of the prostate cancer protein. In this embodiment, either component can be labeled. Thus, e.g., if the competitor is labeled, the presence of label in the wash solution indicates displacement by the agent. Alternatively, if the test compound is labeled, the presence of the label on the support indicates displacement.

In an alternative embodiment, the test compound is added first, with incubation and washing, followed by the competitor. The absence of binding by the competitor may indicate that the test compound is bound to the prostate cancer protein with a higher affinity. Thus, if the test compound is labeled, the presence of the label on the support, coupled with a lack of competitor binding, may indicate that the test compound is capable of binding to the prostate cancer protein.

In a preferred embodiment, the methods comprise differential screening to identity agents that are capable of modulating the activity of the prostate cancer proteins. In this embodiment, the methods comprise combining a prostate cancer protein and a competitor in a first sample. A second sample comprises a test compound, a prostate cancer protein, and a competitor. The binding of the competitor is determined for both samples, and a change, or difference in binding between the two samples indicates the presence of an agent capable of binding to the prostate cancer protein and potentially modulating its activity. That is, if the binding of the competitor is different in the second sample relative to the first sample, the agent is capable of binding to the prostate cancer protein.

Alternatively, differential screening is used to identify drug candidates that bind to the native prostate cancer protein, but cannot bind to modified prostate cancer proteins. The structure of the prostate cancer protein may be modeled, and used in rational drug design to synthesize agents that interact with that site. Drug candidates that affect the activity of a prostate cancer protein are also identified by screening drugs for the ability to either enhance or reduce the activity of the protein.

Positive controls and negative controls may be used in the assays. Preferably control and test samples are performed in at least triplicate to obtain statistically significant results. Incubation of samples is for a time sufficient for the binding of the agent to the protein. Following incubation, samples are washed free of non-specifically bound material and the amount of bound, generally labeled agent determined. For example, where a radiolabel is employed, the samples may be counted in a scintillation counter to determine the amount of bound compound.

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A variety of other reagents may be included in the screening assays. These include reagents like salts, neutral proteins, e.g., albumin, detergents, etc., which may be used to facilitate optimal protein-protein binding and/or reduce non-specific or background interactions. Also reagents that otherwise improve the efficiency of the assay, such as protease inhibitors, nuclease inhibitors, anti-microbial agents, etc., may be used. The mixture of components may be added in an order that provides for the requisite binding.

In a preferred embodiment, the invention provides methods for screening for a compound capable of modulating the activity of a prostate cancer protein. The methods comprise adding a test compound, as defined above, to a cell comprising prostate cancer proteins. Preferred cell types include almost any cell. The cells contain a recombinant nucleic acid that encodes a prostate cancer protein. In a preferred embodiment, a library of candidate agents are tested on a plurality of cells.

In one aspect, the assays are evaluated in the presence or absence or previous or subsequent exposure of physiological signals, e.g., hormones, antibodies, peptides, antigens, cytokines, growth factors, action potentials, pharmacological agents including chemotherapeutics, radiation, carcinogenics, or other cells (e.g., cell-cell contacts). In another example, the determinations are determined at different stages of the cell cycle process.

In this way, compounds that modulate prostate cancer agents are identified.

Compounds with pharmacological activity are able to enhance or interfere with the activity of the prostate cancer protein. Once identified, similar structures are evaluated to identify critical structural feature of the compound.

In one embodiment, a method of inhibiting prostate cancer cell division is provided. The method comprises administration of a prostate cancer inhibitor. In another embodiment, a method of inhibiting prostate cancer or other prostate proliferative condition is provided. The method comprises administration of a prostate cancer inhibitor. In a further embodiment, methods of treating cells or individuals with prostate cancer are provided. The method comprises administration of a prostate cancer inhibitor.

In one embodiment, a prostate cancer inhibitor is an antibody as discussed above. In another embodiment, the prostate cancer inhibitor is an antisense molecule.

A variety of cell growth, proliferation, and metastasis assays are known to those of skill in the art, as described below.

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Soft agar growth or colony formation in suspension

Normal cells require a solid substrate to attach and grow. When the cells are transformed, they lose this phenotype and grow detached from the substrate. For example, transformed cells can grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft agar. The transformed cells, when transfected with tumor suppressor genes, regenerate normal phenotype and require a solid substrate to attach and grow. Soft agar growth or colony formation in suspension assays can be used to identify modulators of prostate cancer sequences, which when expressed in host cells, inhibit abnormal cellular proliferation and transformation. A therapeutic compound would reduce or eliminate the host cells' ability to grow in stirred suspension culture or suspended in semi-solid media, such as semi-solid or soft.

Techniques for soft agar growth or colony formation in suspension assays are described in Freshney (1994) <u>Culture of Animal Cells a Manual of Basic Technique</u> 3d ed. Wiley-Liss, herein incorporated by reference. See also, the methods section of Garkavtsev, et al. (1996), supra, herein incorporated by reference.

Contact inhibition and density limitation of growth

Normal cells typically grow in a flat and organized pattern in a petri dish until they touch other cells. When the cells touch one another, they are contact inhibited and stop growing. When cells are transformed, however, the cells are not contact inhibited and continue to grow to high densities in disorganized foci. Thus, the transformed cells grow to a higher saturation density than normal cells. This can be detected morphologically by the formation of a disoriented monolayer of cells or rounded cells in foci within the regular pattern of normal surrounding cells. Alternatively, labeling index with (³H)-thymidine at saturation density can be used to measure density limitation of growth. See Freshney (1994), supra. The transformed cells, when transfected with tumor suppressor genes, regenerate a normal phenotype and become contact inhibited and would grow to a lower density.

In this assay, labeling index with (²H)-thymidine at saturation density is a preferred method of measuring density limitation of growth. Transformed host cells are transfected with a prostate cancer-associated sequence and are grown for 24 hours at saturation density in non-limiting medium conditions. The percentage of cells labeling with (²H)-thymidine is determined autoradiographically. See, Freshney (1994), supra.

Growth factor or scrum dependence

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Transformed cells have a lower serum dependence than their normal counterparts

(see, e.g., Temin (1966) J. Natl. Cancer Insti. 37:167-175; Eagle, et al. (1970) J. Exp. Med.

131:836-879); Freshney, supra. This is in part due to release of various growth factors by the transformed cells. Growth factor or serum dependence of transformed host cells can be

5 compared with that of control.

Tumor specific markers levels

Tumor cells release an increased amount of certain factors (hereinafter "tumor specific markers"") than their normal counterparts. For example, plasminogen activator (PA) is released from human glioma at a higher level than from normal brain cells (see, e.g., Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) <u>Biological Responses in Cancer</u> Plenum. Similarly, Tumor angiogenesis factor (TAF) is released at a higher level in tumor cells than their normal counterparts. See, e.g., Folkman (1992) <u>Angiogenesis and Cancer. Sem. Cancer Biol.</u>
Various techniques which measure the release of these factors are described in

15 Freshney (1994), supra. Also, see, Unkless, et al. (1974) J. Biol. Chem. 249:4295-4305; Strickland and Beers (1976) J. Biol. Chem. 251:5694-5702; Whur, et al. (1980) Br. J. Cancer 42:305-312; Gullino, "Angiogenesis, tumor vascularization, and potential interference with tumor growth" pp. 178-184 in Mihich (ed. 1985) Biological Responses in Cancer Plenum; and Freshney (1985) Anticancer Res. 5:111-130.

20 Invasiveness into Matrigel

The degree of invasiveness into Matrigel or some other extracellular matrix constituent can be used as an assay to identify compounds that modulate prostate cancer-associated sequences. Tumor cells exhibit a good correlation between malignancy and invasiveness of cells into Matrigel or some other extracellular matrix constituent. In this assay, rumorigenic cells are typically used as host cells. Expression of a tumor suppressor gene in these host cells would decrease invasiveness of the host cells.

Techniques described in Freshney (1994), supra, can be used. Briefly, the level of invasion of host cells can be measured by using filters coated with Matrigel or some other extracellular matrix constituent. Penetration into the gel, or through to the distal side of the filter, is rated as invasiveness, and rated histologically by number of cells and distance moved, or by prelabeling the cells with ¹²⁵I and counting the radioactivity on the distal side of the filter or bottom of the dish. See, e.g., Freshney (1984), supra.

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Tumor growth in vivo

Effects of prostate cancer-associated sequences on cell growth can be tested in transgenic or immune-suppressed mice. Knock-out transgenic mice can be made, in which the prostate cancer gene is disrupted or in which a prostate cancer gene is inserted. Knock-out transgenic mice can be made by insertion of a marker gene or other heterologous gene into the endogenous prostate cancer gene site in the mouse genome via homologous recombination. Such mice can also be made by substituting the endogenous prostate cancer gene with a mutated version of the prostate cancer gene, or by mutating the endogenous prostate cancer gene, e.g., by exposure to carcinogens.

A DNA construct is introduced into the nuclei of embryonic stem cells. Cells containing the newly engineered genetic lesion are injected into a host mouse embryo, which is re-implanted into a recipient female. Some of these embryos develop into chimeric mice that possess germ cells partially derived from the mutant cell line. Therefore, by breeding the chimeric mice it is possible to obtain a new line of mice containing the introduced genetic lesion (see, e.g., Capecchi, et al. (1989) Science 244:1288-1292). Chimeric targeted mice can be derived according to Hogan, et al. (1988) Manipulating the Mouse Embryo: A Laboratory Manual CSH Press; and Robertson (ed. 1987) Teratocarcinomas and Embryonic Stem Cells: A Practical Approach IRL Press, Washington, D.C.

Alternatively, various immune-suppressed or immune-deficient host animals can be used. For example, genetically athymic "nude" mouse (see, e.g., Giovanella, et al. (1974) <u>J. Natl. Cancer Inst.</u> 52:921-930), a SCID mouse, a thymectomized mouse, or an irradiated mouse (see, e.g., Bradley, et al. (1978) <u>Br. J. Cancer</u> 38:263-272; Selby, et al. (1980) <u>Br. J. Cancer</u> 41:52-61) can be used as a host. Transplantable tumor cells (typically about 10⁶ cells) injected into isogenic hosts will produce invasive tumors in a high proportions of cases, while normal cells of similar origin will not. In hosts which developed invasive tumors, cells expressing a prostate cancer-associated sequences are injected subcutaneously. After a suitable length of time, preferably 4-8 weeks, tumor growth is measured (e.g., by volume or by its two largest dimensions) and compared to the control. Tumors that have statistically significant reduction (using, e.g., Student's T test) are said to have inhibited growth.

Polynucleotide modulators of prostate cancer Antisense and RNAi Polynucleotides

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In certain embodiments, the activity of a prostate cancer-associated protein is downregulated, or entirely inhibited, by the use of antisense polynucleotide, i.e., a nucleic acid
complementary to, and which can preferably hybridize specifically to, a coding mRNA
nucleic acid sequence, e.g., a prostate cancer protein mRNA, or a subsequence thereof.
Binding of the antisense polynucleotide to the mRNA reduces the translation and/or stability
of the mRNA.

In the context of this invention, antisense polynucleotides can comprise naturally-occurring nucleotides, or synthetic species formed from naturally-occurring subunits or their close homologs. Antisense polynucleotides may also have altered sugar moieties or intersugar linkages. Exemplary among these are the phosphorothioate and other sulfur containing species which are known for use in the art. Analogs are comprehended by this invention so long as they function effectively to hybridize with the prostate cancer protein mRNA. See, e.g., Isis Pharmaceuticals, Carlsbad, CA; Sequitor, Inc., Natick, MA.

Such antisense polynucleotides can readily be synthesized using recombinant means, or can be synthesized in vitro. Equipment for such synthesis is sold by several vendors, including Applied Biosystems. The preparation of other oligonucleotides such as phosphorothioates and alkylated derivatives is also well known to those of skill in the art.

Antisense molecules as used herein include antisense or sense oligonucleotides.
Sense oligonucleotides can, e.g., be employed to block transcription by binding to the antisense strand. The antisense and sense oligonucleotide comprise a single-stranded nucleic acid sequence (either RNA or DNA) capable of binding to target mRNA (sense) or DNA (antisense) sequences for prostate cancer molecules. A preferred antisense molecule is for a prostate cancer sequences in Tables 1A-4, or for a ligand or activator thereof. Antisense or sense oligonucleotides, according to the present invention, comprise a fragment generally at least about 14 nucleotides, preferably from about 14 to 30 nucleotides. The ability to derive an antisense or a sense oligonucleotide, based upon a cDNA sequence encoding a given protein is described in, e.g., Stein and Cohen (1988) Cancer Res. 48:2659-2668; and van der Krol, et al. (1988) BioTechniques 6:958-976.

RNA interference is a mechanism to suppress gene expression in a sequence specific manner. See, e.g., Brumelkamp, et al. (2002) <u>Sciencexpress</u> (21March2002); Sharp (1999) <u>Genes Dev.</u> 13:139-141; and Cathew (2001) <u>Curr. Op. Cell Biol.</u> 13:244-248. In mammalian cells, short, e.g., 21 nt, double stranded small interfering RNAs (siRNA) have been shown to

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be effective at inducing an RNAi response. See, e.g., Elbashir, et al. (2001) Nature 411:494-498. The mechanism may be used to downregulate expression levels of identified genes, e.g., treatment of or validation of relevance to disease.

5 Ribozymes

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In addition to antisense polynucleotides, ribozymes can be used to target and inhibit transcription of prostate cancer-associated nucleotide sequences. A ribozyme is an RNA molecule that catalytically cleaves other RNA molecules. Different kinds of ribozymes have been described, including group I ribozymes, hammerhead ribozymes, hairpin ribozymes, RNase P, and axhead ribozymes (see, e.g., Castanotto, et al. (1994) Adv. in Pharmacology 25: 289-317 for a general review of the properties of different ribozymes).

The general features of hairpin ribozymes are described, e.g., in Hampel, et al. (1990)

Nucl. Acids Res. 18:299-304; European Patent Publication No. 0 360 257; U.S. Patent No.
5,254,678. Methods of preparing are well known to those of skill in the art. See, e.g., WO
94/26877; Ojwang, et al. (1993) Proc. Natl. Acad. Sci. USA 90:6340-6344; Yamada, et al.
(1994) Human Gene Therapy 1:39-45; Leavitt, et al. (1995) Proc. Natl. Acad. Sci. USA
92:699-703; Leavitt, et al. (1994) Human Gene Therapy 5:1151-120; and Yamada, et al.
(1994) Virology 205:121-126.

Polynucleotide modulators of prostate cancer may be introduced into a cell containing the target nucleotide sequence by formation of a conjugate with a ligand binding molecule, as described in WO 91/04753. Suitable ligand binding molecules include, but are not limited to, cell surface receptors, growth factors, other cytokines, or other ligands that bind to cell surface receptors. Preferably, conjugation of the ligand binding molecule does not substantially interfere with the ability of the ligand binding molecule to bind to its corresponding molecule or receptor, or block entry of the sense or antisense oligonucleotide or its conjugated version into the cell. Alternatively, a polynucleotide modulator of prostate cancer may be introduced into a cell containing the target nucleic acid sequence, e.g., by formation of an polynucleotide-lipid complex, as described in WO 90/10448. It is understood that the use of antisense molecules or knock out and knock in models may also be used in screening assays as discussed above, in addition to methods of treatment.

Thus, in one embodiment, methods of modulating prostate disorders, e.g., cancer in cells or organisms, are provided. In one embodiment, the methods comprise administering to

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a patient, e.g., to a cell within the patient, an anti-prostate cancer antibody that reduces or eliminates the biological activity of an endogenous prostate cancer protein. Alternatively, the methods comprise administering to a cell or organism a recombinant nucleic acid encoding a prostate cancer protein. This may be accomplished in many ways. In a preferred embodiment, e.g., when the prostate cancer sequence is down-regulated in prostate cancer, such state may be reversed by increasing the amount of prostate cancer gene product in the cell. This can be accomplished, e.g., by overexpressing the endogenous prostate cancer gene or administering a gene encoding the prostate cancer sequence, using known gene-therapy techniques, e.g.. In a preferred embodiment, the gene therapy techniques include the incorporation of the exogenous gene using enhanced homologous recombination (EHR), e.g., as described in PCT/US93/03868, hereby incorporated by reference in its entirety.

Alternatively, e.g., when the prostate cancer sequence is up-regulated in prostate cancer, the activity of the endogenous prostate cancer gene is decreased, e.g., by the administration of a prostate cancer antisense nucleic acid.

In one embodiment, the prostate cancer proteins of the present invention may be used to generate polyclonal and monoclonal antibodies to prostate cancer proteins. Similarly, the prostate cancer proteins can be coupled, using standard technology, to affinity chromatography columns. These columns may then be used to purify prostate cancer antibodies useful for production, diagnostic, or therapeutic purposes. In a preferred embodiment, the antibodies are generated to epitopes unique to a prostate cancer protein; that is, the antibodies show little or no cross-reactivity to other proteins. The prostate cancer antibodies may be coupled to standard affinity chromatography columns and used to purify prostate cancer proteins. The antibodies may also be used as blocking polypeptides, as outlined above, since they will specifically bind to the prostate cancer protein.

Methods of identifying variant prostate cancer-associated sequences

Without being bound by theory, expression of various prostate cancer sequences is correlated with prostate cancer or other prostate disorders. Accordingly, disorders based on mutant or variant prostate cancer genes may be determined. In one embodiment, the invention provides methods for identifying cells containing variant prostate cancer genes, e.g., determining all or part of the sequence of at least one endogenous prostate cancer genes in a cell. This may be accomplished using many sequencing techniques. In a preferred

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embodiment, the invention provides methods of identifying the prostate cancer genotype of an individual, e.g., determining all or part of the sequence of at least one prostate cancer gene of the individual. This is generally done in at least one tissue of the individual, and may include the evaluation of a number of tissues or different samples of the same tissue. The method may include comparing the sequence of the sequenced prostate cancer gene to a known prostate cancer gene, e.g., a wild-type gene.

The sequence of all or part of the prostate cancer gene can then be compared to the sequence of a known prostate cancer gene to determine if differences exist. This can be done using many known homology programs, such as Bestfit, etc. In a preferred embodiment, the presence of a difference in the sequence between the prostate cancer gene of the patient and the known prostate cancer gene correlates with a disease state or a propensity for a disease state, as outlined herein.

In a preferred embodiment, the prostate cancer genes are used as probes to determine the number of copies of the prostate cancer gene in the genome.

In another preferred embodiment, the prostate cancer genes are used as probes to determine the chromosomal localization of the prostate cancer genes. Information such as chromosomal localization finds use in providing a diagnosis or prognosis in particular when chromosomal abnormalities such as translocations, and the like are identified in the prostate cancer gene locus.

Administration of pharmaceutical and vaccine compositions

In one embodiment, a therapeutically effective dose of a prostate cancer protein or modulator thereof, is administered to a patient. By "therapeutically effective dose" herein is meant a dose that produces effects for which it is administered. The exact dose will depend on the purpose of the treatment, and will be ascertainable by one skilled in the art using known techniques (e.g., Ansel, et al. (1992) Pharmaceutical Dosage Forms and Drug Delivery; Lieberman (1993) Pharmaceutical Dosage Forms (vols. 1-3, Dekker, ISBN 0824770846, 082476918X, 0824712692, 0824716981; Lloyd (1999) The Art, Science and Technology of Pharmaceutical Compounding Amer. Pharma. Assn.; and Pickar (1999) Dosage Calculations Thomson). Adjustments for prostate cancer degradation, systemic versus localized delivery, and rate of new protease synthesis, as well as the age, body weight, general health, sex, diet, time of administration, drug interaction, and the severity of the

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condition may be necessary, and will be ascertainable with routine experimentation by those skilled in the art. U.S. Patent Application N. 09/687,576 further discloses the use of compositions and methods of diagnosis and treatment in prostate cancer is hereby expressly incorporated by reference.

A "patient" for the purposes of the present invention includes both humans and other animals, particularly mammals. Thus the methods are applicable to both human therapy and veterinary applications. In the preferred embodiment the patient is a mammal, preferably a primate, and in the most preferred embodiment the patient is human. The patient typically will suffer from a prostate proliferative disorder, e.g., malignant or non-malignant, and may include cancer of other related conditions or disorders.

The administration of the prostate cancer proteins and modulators thereof of the present invention can be done in a variety of ways as discussed above, including, but not limited to, orally, subcutaneously, intravenously, intranasally, transdermally, intraperitoneally, intramuscularly, intrapulmonary, vaginally, rectally, or intraocularly. In some instances, e.g., in the treatment of wounds and inflammation, the prostate cancer proteins and modulators may be directly applied as a solution or spray, or via catheter.

The pharmaceutical compositions of the present invention comprise a prostate cancer protein in a form suitable for administration to a patient. In the preferred embodiment, the pharmaceutical compositions are in a water soluble form, such as being present as pharmaceutically acceptable salts, which is meant to include both acid and base addition salts. "Pharmaceutically acceptable acid addition salt" refers to those salts that retain the biological effectiveness of the free bases and that are not biologically or otherwise undesirable, formed with inorganic acids such as hydrochloric acid, hydrobromic acid, sulfuric acid, nitric acid, phosphoric acid and the like, and organic acids such as acetic acid. propionic acid, glycolic acid, pyruvic acid, oxalic acid, maleic acid, malonic acid, succinic acid, fumaric acid, tartaric acid, citric acid, benzoic acid, cinnamic acid, mandelic acid, methanesulfonic acid, ethanesulfonic acid, p-toluenesulfonic acid, salicylic acid, and the like. "Pharmaceutically acceptable base addition salts" include those derived from inorganic bases such as sodium, potassium, lithium, ammonium, calcium, magnesium, iron, zinc, copper, manganese, aluminum salts, and the like. Particularly preferred are the ammonium, potassium, sodium, calcium, and magnesium salts. Salts derived from pharmaceutically acceptable organic non-toxic bases include salts of primary, secondary, and tertiary amines,

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substituted amines including naturally occurring substituted amines, cyclic amines and basic ion exchange resins, such as isopropylamine, trimethylamine, diethylamine, triethylamine, tripropylamine, and ethanolamine.

The pharmaceutical compositions may also include one or more of the following: carrier proteins such as serum albumin; buffers; fillers such as microcrystalline cellulose, lactose, corn and other starches; binding agents; sweeteners and other flavoring agents; coloring agents; and polyethylene glycol.

The pharmaceutical compositions can be administered in a variety of unit dosage forms depending upon the method of administration. For example, unit dosage forms suitable for oral administration include, but are not limited to, powder, tablets, pills, capsules and lozenges. It is recognized that prostate cancer protein modulators (e.g., antibodies, antisense constructs, ribozymes, small organic molecules, etc.) when administered orally, should be protected from digestion. This is typically accomplished either by complexing the molecule(s) with a composition to render it resistant to acidic and enzymatic hydrolysis, or by packaging the molecule(s) in an appropriately resistant carrier, such as a liposome or a protection barrier. Means of protecting agents from digestion are well known in the art.

The compositions for administration will commonly comprise a prostate cancer protein modulator dissolved in a pharmaceutically acceptable carrier, preferably an aqueous carrier. A variety of aqueous carriers can be used, e.g., buffered saline and the like. These solutions are typically sterile and generally free of undesirable matter. These compositions may be sterilized by conventional, well known sterilization techniques. The compositions may contain pharmaceutically acceptable auxiliary substances as required to approximate physiological conditions such as pH adjusting and buffering agents, toxicity adjusting agents and the like, e.g., sodium acetate, sodium chloride, potassium chloride, calcium chloride, sodium lactate, and the like. The concentration of active agent in these formulations can vary widely, and will be selected primarily based on fluid volumes, viscosities, body weight, and the like in accordance with the particular mode of administration selected and the patient's needs (e.g., (1980) Remington's Pharmaceutical Science (15th ed.); and Hardman, et al. (eds. 2001) Goodman & Gilman: The Pharmacological Basis of Therapeutics McGraw-Hill.

Thus, a typical pharmaceutical composition for intravenous administration would be about 0.1 to 10 mg per patient per day. Dosages from 0.1 up to about 100 mg per patient per day may be used, particularly when the drug is administered to a secluded site and not into

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the blood stream, such as into a body cavity or into a lumen of an organ. Substantially higher dosages are possible in topical administration. Actual methods for preparing parenterally administrable compositions will be known or apparent to those skilled in the art, e.g., Remington's Pharmaceutical Science and Goodman and Gilman: The Pharmacological Basis of Therapeutics, supra.

The compositions containing modulators of prostate cancer proteins can be administered for therapeutic or prophylactic treatments. In therapeutic applications, compositions are administered to a patient suffering from a disease (e.g., a cancer) in an amount sufficient to cure or at least partially retard or arrest the disease and its complications. An amount adequate to accomplish this is defined as a "therapeutically effective dose." Amounts effective for this use will depend upon the severity of the disease and the general state of the patient's health. Single or multiple administrations of the compositions may be administered depending on the dosage and frequency as required and tolerated by the patient. The composition should provide a sufficient quantity of the agents of this invention to effectively treat the patient. An amount of modulator that is capable of preventing or slowing the development of cancer in a mammal is referred to as a "prophylactically effective dose." The particular dose required for a prophylactic treatment will depend upon the medical condition and history of the mammal, the particular cancer being prevented, as well as other factors such as age, weight, gender, administration route, efficiency, etc. Such prophylactic treatments may be used, e.g., in a mammal who has previously had cancer to prevent a recurrence of the cancer, or in a mammal who is suspected of having a significant likelihood of developing cancer, e.g., based partly on gene expression profiles.

It will be appreciated that the present prostate cancer protein-modulating compounds can be administered alone or in combination with additional prostate cancer modulating compounds or with other therapeutic agent, e.g., other anti-cancer agents or treatments.

In numerous embodiments, one or more nucleic acids, e.g., polynucleotides comprising nucleic acid sequences set forth in Tables 1A-4such as antisense polynucleotides, silencing RNA, or ribozymes, will be introduced into cells, in vitro or in vivo. The present invention provides methods, reagents, vectors, and cells useful for expression of prostate cancer-associated polypeptides and nucleic acids using in vitro (cell-free), ex vivo or in vivo (cell or organism-based) recombinant expression systems.

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The particular procedure used to introduce the nucleic acids into a host cell for expression of a protein or nucleic acid is application specific. Many procedures for introducing foreign nucleotide sequences into host cells may be used. These include the use of calcium phosphate transfection, spheroplasts, electroporation, liposomes, microinjection, plasma vectors, viral vectors, and many other well known methods for introducing cloned genomic DNA, cDNA, synthetic DNA, or other foreign genetic material into a host cell (see, e.g., Berger and Kimmel (1987) <u>Guide to Molecular Cloning Techniques from Methods in Enzymology</u> (vol. 152) Academic Press; Ausubel, et al., (eds. supplemented through 1999) <u>Current Protocols</u> Lippincott; and Sambrook, et al. (1989) <u>Molecular Cloning: A Laboratory Manual</u> (2d ed., Vol. 1-3) CSH Press.

In a preferred embodiment, prostate cancer proteins and modulators are administered as therapeutic agents, and can be formulated as outlined above. Similarly, prostate cancer genes (including both the full-length sequence, partial sequences, or regulatory sequences of the prostate cancer coding regions) can be administered in a gene therapy application. These prostate cancer genes can include antisense applications, either as gene therapy (i.e., for incorporation into the genome) or as antisense compositions, as will be appreciated by those in the art.

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Prostate cancer polypeptides and polynucleotides can also be administered as vaccine compositions to stimulate HTL, CTL, and antibody responses.. Such vaccine compositions can include, e.g., lipidated peptides (see, e.g., Vitiello, et al. (1995) J. Clin. Invest. 95:341-349), peptide compositions encapsulated in poly(DL-lactide-co-glycolide) ("PLC") microspheres (see, e.g., Eldridge, et al. (1991) Molec. Immunol, 28:287-294; Alonso, et al. (1994) Vaccine 12:299-306; Jones, et al. (1995) Vaccine 13:675-681), peptide compositions contained in immune stimulating complexes (ISCOMS) (see, e.g., Takahashi, et al. (1990) Nature 344:873-875; Hu, et al. (1998) Clin Exp Immunol. 113:235-243), multiple antigen peptide systems (MAPs) (see, e.g., Tam (1988) Proc. Natl. Acad. Sci. USA 85:5409-5413; Tam (1996) J. Immunol. Methods 196:17-32), peptides formulated as multivalent peptides; peptides for use in ballistic delivery systems, typically crystallized peptides, viral delivery vectors (Perkus, et al., p. 379, in Kaufmann (ed. 1996) Concepts in vaccine development de Gruyter; Chakrabarti, et al. (1986) Nature 320:535-537; Hu, et al. (1986) AIDS Bio/Technology 4:790-xxx; Top, et al. (1971) J. Infect. Dis. 124:148-154; Chanda, et al. (1990) Virology 175:535-547), particles of viral or synthetic

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origin (see, e.g., Kofler, et al. (1996) J. Immunol. Methods 192:25-35; Eldridge, et al. (1993) Sem. Hematol. 30:16-24; Falo, et al. (1995) Nature Med. 7:649-653), adjuvants (Warren, et al. (1986) Annu. Rev. Immunol. 4:369-388; Gupta, et al. (1993) Yaccine 11:293-306), liposomes (Reddy, et al. (1992) J. Immunol. 148:1585-1589; Rock (1996) Immunol. Today 17:131-137), or, naked or particle absorbed cDNA (Ulmer, et al. (1993) Science 259:1745-1749; Robinson, et al. (1993) Yaccine 11:957-960; Shiver, et al., p. 423, in Kaufmann (ed. 1996) Concepts in Vaccine Development de Gruyter; Cease and Berzofsky (1994) Annu. Rev. Immunol. 12:923-989; and Eldridge, et al. (1993) Sem. Hematol. 30:16-24). Toxintargeted delivery technologies, also known as receptor mediated targeting, such as those of Avant Immunotherapeutics. Inc. (Needham, Massachusetts) may also be used.

Vaccine compositions often include adjuvants. Many adjuvants contain a substance designed to protect the antigen from rapid catabolism, such as aluminum hydroxide or mineral oil, and a stimulator of immune responses, such as lipid A, Bortadella pertussis or Mycobacterium tuberculosis derived proteins. Certain adjuvants are commercially available as, e.g., Freund's Incomplete Adjuvant and Complete Adjuvant (Difco Laboratories, Detroit, MI); Merck Adjuvant 65 (Merck and Company, Inc., Rahway, NJ); AS-2 (SmithKline Beecham, Philadelphia, PA); aluminum salts such as aluminum hydroxide gel (alum) or aluminum phosphate; salts of calcium, iron or zinc; an insoluble suspension of acylated tyrosine; acylated sugars; cationically or anionically derivatized polysaccharides; polyphosphazenes; biodegradable microspheres; monophosphoryl lipid A, and quil A. Cytokines, such as GM-CSF, interleukin-2, -7, -12, and other like growth factors, may also be used as adjuvants.

Vaccines can be administered as nucleic acid compositions wherein DNA or RNA encoding one or more of the polypeptides, or a fragment thereof, is administered to a patient. This approach is described, for instance, in Wolff, et al. (1990) Science 247:1465-1468 as well as U.S. Patent Nos. 5,580,859; 5,589,466; 5,804,566; 5,739,118; 5,736,524; 5,679,647; WO 98/04720; and in more detail below. Examples of DNA-based delivery technologies include "naked DNA", facilitated (bupivicaine, polymers, peptide-mediated) delivery, cationic lipid complexes, and particle-mediated ("gene gun") or pressure-mediated delivery (see, e.g., U.S. Patent No. 5,922,687).

For therapeutic or prophylactic immunization purposes, the peptides of the invention can be expressed by viral or bacterial vectors. Examples of expression vectors include

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attenuated viral hosts, such as vaccinia or fowlpox. This approach involves the use of vaccinia virus, e.g., as a vector to express nucleotide sequences that encode prostate cancer polypeptides or polypeptide fragments. Upon introduction into a host, the recombinant vaccinia virus expresses the immunogenic peptide, and thereby elicits an immune response. Vaccinia vectors and methods useful in immunization protocols are described in, e.g., U.S. Patent No. 4,722,848. Another vector is BCG (Bacille Calmette Guerin). BCG vectors are described in Stover, et al. (1991) Nature 351:456-460. A wide variety of other vectors useful for therapeutic administration or immunization, e.g., adeno and adeno-associated virus vectors, retroviral vectors, Salmonella typhi vectors, detoxified anthrax toxin vectors, and the like, will be apparent to those skilled in the art from the description herein (see, e.g., Shata, et al. (2000) Mol. Med. Today 6:66-71; Shedlock, et al. (2000) J. Leuk. Biol. 68:793-806; Hipp, et al. (2000) In Vivo 14:571-85).

Methods for the use of genes as DNA vaccines are well known, and include placing a prostate cancer gene or portion of a prostate cancer gene under the control of a regulatable promoter or a tissue-specific promoter for expression in a prostate cancer patient. The prostate cancer gene used for DNA vaccines can encode full-length prostate cancer proteins, but more preferably encodes portions of the prostate cancer proteins including peptides derived from the prostate cancer protein. In one embodiment, a patient is immunized with a DNA vaccine comprising a plurality of nucleotide sequences derived from a prostate cancer gene. For example, prostate cancer-associated genes or sequence encoding subfragments of a prostate cancer protein are introduced into expression vectors and tested for their immunogenicity in the context of Class I MHC and an ability to generate cytotoxic T cell responses. This procedure may provide for production of cytotoxic T lymphocyte responses against cells which present antigen, including intracellular epitopes.

In a preferred embodiment, the DNA vaccines include a gene encoding an adjuvant molecule with the DNA vaccine. Such adjuvant molecules include cytokines that increase the immunogenic response to the prostate cancer polypeptide encoded by the DNA vaccine. Additional or alternative adjuvants are available.

In another preferred embodiment prostate cancer genes find use in generating animal models of prostate cancer. When the prostate cancer gene identified is repressed or diminished in cancer tissue, gene therapy technology, e.g., wherein antisense RNA directed to the prostate cancer gene will also diminish or repress expression of the gene. Animal

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models of prostate cancer find use in screening for modulators of a prostate cancer-associated sequence or modulators of prostate cancer. Similarly, transgenic animal technology including gene knockout technology, e.g., as a result of homologous recombination with an appropriate gene targeting vector, will result in the absence or increased expression of the prostate cancer protein. When desired, tissue-specific expression or knockout of the prostate cancer protein may be necessary.

It is also possible that the prostate cancer protein is overexpressed in prostate cancer. As such, transgenic animals can be generated that overexpress the prostate cancer protein. Depending on the desired expression level, promoters of various strengths can be employed to express the transgene. Also, the number of copies of the integrated transgene can be determined and compared for a determination of the expression level of the transgene. Animals generated by such methods find use as animal models of prostate cancer and are additionally useful in screening for modulators to treat prostate cancer.

15 Kits for Use in Diagnostic and/or Prognostic Applications

For use in diagnostic, research, and therapeutic applications suggested above, kits are also provided by the invention. In the diagnostic and research applications such kits may include one of the following: assay reagents, buffers, prostate cancer-specific nucleic acids or antibodies, hybridization probes and/or primers, antisense polynucleotides, silencing RNA, ribozymes, dominant negative prostate cancer polypeptides or polynucleotides, small molecules inhibitors of prostate cancer-associated sequences, etc. A therapeutic product may include sterile saline or another pharmaceutically acceptable emulsion and suspension base.

In addition, the kits may include instructional materials containing instructions (i.e., protocols) for the practice of the methods of this invention. While the instructional materials typically comprise written or printed materials they are not limited to such. A medium capable of storing such instructions and communicating them to an end user is contemplated by this invention. Such media include, but are not limited to electronic storage media (e.g., magnetic discs, tapes, cartridges, chips), optical media (e.g., CD ROM), and the like. Such media may include addresses to internet sites that provide such instructional materials.

The present invention also provides for kits for screening for modulators of prostate cancer-associated sequences. Such kits can be prepared from readily available materials and reagents. For example, such kits can comprise one or more of the following materials: a

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prostate cancer-associated polypeptide or polynucleotide, reaction tubes, and instructions for testing prostate cancer-associated activity. Optionally, the kit contains biologically active prostate cancer protein. A wide variety of kits and components can be prepared according to the present invention, depending upon the intended user of the kit and the particular needs of the user. Diagnosis would typically involve evaluation of a plurality of genes or products. The genes will be selected based on correlations with important parameters in disease which may be identified in historical or outcome data.

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EXAMPLES

Example 1: Gene Chip Analyses of Expression Profiles

Molecular profiles of various normal and cancerous tissues were determined and analyzed using gene chips. RNA was isolated and gene chip analysis was performed as described (Glynne, et al. (2000) Nature 403:672-676; Zhao, et al. (2000) Genes Dev. 14:981-993).

EXAMPLE 2: Identification of androgen dependent/independent genes

To identify gene expression changes during the transition from androgen-dependent to androgen-independent prostate cancer, oligonucleotide microarrays ("K" chips or Affymetrix Eos Hu03) were interrogated with cRNAs derived from the human CWR22 prostate cancer xenograft model propagated in nude mice (Pretlow, et al. (1993) <u>J. Natl. Cancer Inst.</u> 85:394-398). The CWR22 xenograft is androgen-dependent when grown in male Nude mice. Androgen-independent sub-lines can be derived by first establishing androgen-dependent tumors in male mice. The mice are then castrated to remove the primary source of growth stimulus (androgen), resulting in tumor regression. Within 3-10 months molecular events prompt the tumors to relapse and start growing as androgen-independent tumors. See, e.g., Nagabhushan, et al. (1996) <u>Cancer Res.</u> 56:3042-3046; Amler, et al. (2000) <u>Cancer Res.</u> 60:6134-6141: and Bubendorf, et al. (1999) J. Natl. Cancer Inst. 91:1758-1764.

Using the CWR22 xenograft model, tumors were grown subcutaneously in male nude mice. Tumors were harvested at different times after castration. The time points post-castration included (in days): 0, 1, 3, 4, 5, 10, 30, 40, 50, 51, 52, 59, 60, 61, 70, 79, 80, 82, 120, and 125. Analyses also included established androgen-independent xenografts. Castration resulted in tumor regression. At day 120 and thereafter, the tumors relapsed and started growing in the absence of androgen.

cRNAs were generated by in vitro transcription assays (IVTs) from the different samples and were hybridized to the oligonucleotide microarrays (Affymetrix Eos Hu03). Hybridization was measured by the average fluorescence intensity (AI), which is directly proportional to the expression level of the gene.

Two types of analyses were applied to the results: Analysis A:

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The samples were divided into different time groups which included the following time points post castration (in days): 1-5, 10, 30-40, 50-82, 120-125. To identify changes in gene expression, the following calculations were made:

- The median (or mean, in case there were only 2 samples in a group) was calculated for each group.
- 2. The medians (or means) for each group was compared to one-another.
- Genes were selected that exhibited a minimum 2 fold difference in the median (or mean) between any of the groups.
- The change in gene expression over time was analyzed for each selected gene to look for specific pattern changes.

Only genes with an interesting expression pattern during the androgen-ablation time course were selected as potential new therapeutic targets and/or diagnostic markers. Among the 70,000 gene clusters present on Hu01 and Hu02, we identified 820 gene clusters with the desired expression patterns. These expression patterns can be broadly defined into the

- 15 following categories:
 - Genes that are expressed early in the time course, then drop off in expression, and then express again with emergence of androgen-independence (hi-lo-hi pattern in Table 1A).
 - Genes that are expressed early in the time course, then drop off in expression, and do not express again with emergence of androgen-independence (hi-lo-lo pattern in Table 1A).
- Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-lo-hi pattern in Table 1A).
 - Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-hi-hi pattern in Table 1A).
- Genes that are not expressed early in the time course, but then express as androgen is
 withdrawn and drop off again with emergence of androgen-independence (lo-hi-lo pattern in
 Table 1A).

Group 1 is characterized by cell-cycle regulating genes, such as those encoding cyclin B1, p21/WAF1, CDC18-homolog, cyclin A2, cyclin D1, and possible growth factors such as hAG2 (anterior gradient 2 homolog) among others. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group 1 genes good targets for treating advanced prostate cancer.

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Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141).

Group 3 represents genes that are up-regulated by signals that induce the androgenindependent phenotype. This group includes genes encoding stamnocalcin 2, c-fos protooncogene product, vascular endothelial growth factor, the cell surface protein transmembrane
4 superfamily member 1 and adrenomedullin among others. Adrenomedullin has recently
been shown to act as an autocrine growth factor for the androgen-independent prostate cancer
cell line DU145 (Rocchi, et al. (2001) <u>Cancer Res.</u> 61:1196-1206), indicating that its upregulation is critical for supporting an androgen-independent phenotype. Blocking
adrenomedullin function, and/or other genes in this group, prevents the growth of androgenindependent turnor cells.

Group 4 represents genes that are androgen-repressed and are only expressed in the absence of androgen. This group includes genes encoding the protein tyrosine phosphatase interacting protein liprin-alpha 2, the CD24 antigen, and the catalytic subunit for phosphatidylinositol 4-kinase amongst others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 4. Therefore, Group 4 gene products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Group 5 represents genes that are involved in regulating signals that induce an androgen-independent phenotype. This group includes genes encoding Rab2 (a Ras-like G protein), the Son of Sevenless homolog (a GTP/GDP exchange factor involved in activating Ras-like proteins), and the p85 regulatory subunit for phosphoinositide-3-kinase (P13-kinase). The P13-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) <u>Cancer Res.</u> 59:2891-2897). This indicates that ras-like signals and signals dependent on P13-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 5 gene products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Analysis B:

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For the second analysis, the samples were divided into 4 time groups which included the following time points post castration (in days): 0-1, 3-5, 10-82, >120. To identify changes in gene expression, the following analysis was performed:

- 1. Genes were selected that exhibited a minimum of 100 AI units at the 90^{th} percentile
- expression level of samples.
 - The group mean expression levels for each gene were calculated. The genes were further sub-selected to exhibit a minimum 3 fold difference between the group means.
 - 3. An analysis of variance was then performed on selected genes. From the original 59,680 gene clusters present on the Hu03 gene chip, only about 1165 genes with a P value of < 0.01 were identified that also exhibited the above mentioned parameters.</p>
 - 4. A method was then employed for calculating the positive false discovery rate (pFDR), i.e., an estimate of the proportion of false-positives present in a set of findings (Storey and Tibshirani (2001) Technical Report, Department of Statistics, Stanford University, CA).
 This technique was developed explicitly for use with microarray data. The procedure
- 15 involves randomly assigning the membership status of each sample to a group and reperforming the analysis of variance. In each simulation, the number of group members (6 for Group 1, 9 for group 2, 15 for group 3, and 4 for group 4) remained constant, but these designations were shuffled and assigned to each sample at random. The permutation was performed 1000 times, and for each simulation, the number of findings at P < 0.01 was noted.</p>
- 20 The number of false positives under null conditions, was then divided by the number of actual findings (n=1165 genes) to obtain an estimate of the proportion of false positive findings. After the application of a correction factor, the final estimate for the pFDR was about 1%. Thus, one can expect that approximately 12 of the 1165 findings are false positives.
- 5. The approximately 1165 genes were clustered by expression pattern to identify specific pattern changes. Only genes with an interesting expression pattern during the androgenablation time course were selected as potential new therapeutic targets and/or diagnostic markers. These expression patterns can be broadly defined into the following categories:
 - 1. Genes that are expressed early in the time course of androgen withdrawal, then drop off in
- 30 expression, and then express again with emergence of androgen-independence (hi-lo-lo-hi pattern in Table 2A).

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conditions.

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Genes that are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgenindependence (hi-lo-lo-lo pattern in Table 2A).

- Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of androgen-
- independence (hi-hi-lo-lo pattern in Table 2A).

 4. Genes that are not expressed early in the time course, but express only with emergence of
- androgen-independence (10-10-10-hi pattern in Table 2A).

 5. Genes that are not expressed early in the time course, but then express as androgen is
- withdrawn and continue to express with emergence of androgen-independence (lo-lo-hi-hi pattern in Table 2A).
 - Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (lo-lo-hi-lo pattern in Table 2A).

Group 1 is characterized by cell-cycle regulating genes and cell growth promoting

genes, such as those encoding cyclin B1 and CDC45 among others, growth factors/hormones such as hAG2 (anterior gradient 2 homolog), adrenomedullin, and stanniocalcin 2 among others, and growth factor receptors, such as the bone morphogenic protein receptor type 1B (BMP-R1B) and the endothelial differentiation lysophosphatidic acid G-protein-coupled receptor 7 among others. Adrenomedullin has recently been shown to act as an autocrine growth factor for the androgen-independent prostate cancer cell line DU145 (Rocchi, et al. (2001) Cancer Res. 61:1196-1206), indicating that its up-regulation is critical for supporting an androgen-independent phenotype. This indicates that interruption of growth factor and/or cell cycle pathways prevents the emergence of androgen-independent disease, making group 1 genes good targets for treating both localized and advanced prostate cancer and related

Group 2 represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as the endothelial protein C receptor (EPCR) and the potassium intermediate/small conductance calcium-activated channel (subfamily N, member 2). These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

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Group 3 also represents genes that are androgen-dependent, and do not re-express due to the lack of androgen signal in the androgen-independent phenotype. This group includes genes encoding proteins such as Fibronectin 1, which has been previously shown to be down-regulated with androgen-withdrawal (Amler, et al. (2000) Cancer Res. 60:6134-6141), and genes encoding signaling proteins such as Rho GTPase activating protein 1. These genes represent targets for treating androgen-dependent prostate cancer and related conditions.

Group 4 represents genes that are up-regulated by signals that induce and maintain the androgen-independent phenotype. This group includes genes encoding potential growth promoting proteins such as chemokine-like factor (Unigene ID Hs.15159), colon cancer-associated protein Mic1, and the mitogen-activated protein kinase-activated protein kinase 2. Blocking function of these proteins, and/or other genes in this group, prevents the growth of androgen-independent tumor cells and related conditions.

Group 5 represents genes that are androgen-repressed and are only expressed in the absence of androgen or that are induced by the absence of androgen. This group includes genes encoding transcriptional regulators such as the androgen receptor, the DNA activated protein kinase (catalytic subunit), and nuclear factor related to kappa B binding protein (NFRKB), among others. Patients that are treated for advanced prostate cancer by hormone-ablation may have in their bodies cells that have survived hormone-ablation and are likely to up-regulate genes that belong to Group 5. Therefore, Group 5 gene products are particularly good therapeutic targets for treating patients undergoing hormone-ablation therapy.

Group 6 represents genes that are involved in regulating signals that are induced during androgen withdrawal and that induce an androgen-independent phenotype. This group includes genes encoding signaling molecules such as phosphoinositide-3-kinase (class 2, alpha polypeptide), signal transducer and activator of transcription 2 (STAT2), phospholipase A2 (group IIA) and the protein tyrosine phosphatase interacting protein liprin-alpha 2, cell surface receptors such as gamma-aminobutyric acid (GABA) A receptor epsilon subunit, G protein-coupled receptor 48, and immune function proteins such as the major histocompatibility complex class II DR alpha. The PI3-kinase pathway has been implicated in providing a survival signal to the prostate cancer cell line LNCaP (Lin, et al. (1999) <u>Cancer</u> Res. 59:2891-2897). This indicates that ras-like signals and signals dependent on PI3-kinase are involved in inducing the androgen-independent phenotype. For that reason, Group 6 gene

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products are particularly good therapeutic targets for treating patients undergoing hormoneablation therapy. WO 02/098358 PCT/US02/17594

TABLE 16 provides Acceptation unchange for genes, including personed reciprocol loss, plicotropostated in their entable, here not throughout the application where Acceptation returned as any provided, Content with an interching expension patient and their being heard groups and provided in their expension patients. These expression patients can be broatly defined in this fact in the factoring callengation. I Content their amentments daily in their concess, then deep representation patients are subject to the content of the factoring callengation. Content their amentments of their patients are subject to the content of their patients and their patients are subject to the content of their patients. I content their amentments of their patients are content of their patients. I content their content of their patients are content of their patients. The content of their patients are content of their patients are content of their patients are content to their patients are content to their patients. The content of their patients are content to their

- hi pattern).
- in position.

 5. Gones that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen-independence (ic-hi-lo 10
 - pattern). Table (Billets accession numbers for primekeys lacking a uniquend D in table 14. For each probased is listed a gene cluster number from which dignosciolides were designed. Gene clusters were complict using sequences deri
- 15 Table 1C lists genomic positioning for primekeys lacking uniquese ID's and accession numbers in tables 1A. For each predicted exon is listed genomic sequence source used for prediction. Nucleotide locations of each predicted exon are also listed.

	TABLE 1A				
20	Pkey	ExApon	UnigenelD	Unigene Title	patiern
	102772	U83115 N48373	Hs.161002 Hs.10247	absent in melanoma 1 eclivated leuccoyte cell adhesion molecu	hì-lo-hì hi-lo-hi
	102276	N48373	Hs.10247	activated feucocyte cell adhesion molecu	hi-lo-hi
25	100654	A03758	NS.10247	activates resouchie del apricador indeco	hi-lo-hi
23	100656	A03758			hi-lo-hi
	135400	X78592	Hs.99915	androgen receptor (dihydrolestosterone r	hi-lo-hi
	331363	AW582256	"Hs.91011	anterior gradient 2 (Xenepus laevis) hom	hi-lo-hi
	115764	AW582256	"Hs.91011	anterior gradient 2 (Xenepus laevis) hom	hi-lo-hi
30	120483	BE251623	Hs.1578	baculoviral IAP repeat-containing 5 (sur	hi-lo-hi
	101505	AA307680	Hs.75692	asparagine synthelase	hi-lo-hi
	127236	AW661857	Hs.98658	budding uninhibited by benzimidazoles 1	hi-lo-hi
	128472	BE241880	"Hs.10029	cathepsin C	hi-lo-hi
	102712	U77949	Hs.69563	CDC6 (cell division cycle 6, S. cerevisi	hì-lo-hì
35	314943	Y00272	Hs.184572	cell division cycle 2. G1 to S and G2 to	hi-lo-hi
	102123	NM_001809	"Hs.1594	centromere protein A (17kD)	hi-lo-hi
	326213			CH. 17_hs gi[5867224	hì-lo-hi
	327110			CH.21_hs gil6117842	hi-lo-hi
40	339186			CH22_DA59H18.GENSCAN.72-13	hi-lo-hi
40	337755			CH22_EM:AC000097.GENSCAN.109-2	hì-lo-hì
	337674			CH22_EM:AC000097.GENSCAN:67-4	hi-lo-hi
	337675			CH22_EMAC000097.GENSCAN.67-6	hi-lo-hi
	333516			CH22_FGENES.173_1	hi-lo-hi
45	333517			CH22_FGENES.173_2	hi-lo-hi hi-lo-hi
43	333795			CH22_FGENES.275_1	
	333796 333808			CH22_FGENES.275_3 CH22_FGENES.279_2	hi-lo-hi hi-lo-hi
	333809			CH22_FGENES.279_2 CH22_FGENES.280_2	hi-to-hi
	-332792			CH22_FGENES3.20 CH22_FGENES3.2	hi-lo-hi
50	334101			CH22_FGENES.327_59	hi-lo-hi
٥٠.	334502			CH22_FGENES.397_18	hi-to-hi
-	334616			CH22_FGENES.411_15	hì-lo-hì
	334899			CH22_FGENES 452_13	hl-lo-hi
	334900			CH22 FGENES.452 14	hi-to-hi
5.5	334902			CH22 FGENES.452_16	hi-lo-hi
	334905			CH22_FGENES.452_20	hl-to-hi
	334906			CH22_FGENES.452_21	hi-to-hi
	334951			CH22_FGENES.465_20	hì-lo-hi
	335044			CH22_FGENES.480_1	hi-to-hi
60	335753			CH22_FGENES.604_2	hi-lo-hi
	335755			CH22_FGENES.604_4	hi-lo-hi
	333135			CH22_FGENES.83_11	ht-lo-hi
	333137			CH22_FGENES.83_13	hi-lo-hi
65	333138			CH22_FGENES.83_15	hì-lo-hi
03	333139			CH22_FGENES.83_16	hi-lo-hi
	336721	AF098158	11-0000	CH22_FGENES.83-17	hi-lo-hi
	105012		Hs.9329	chromosome 20 open reading frame 1	hì-lo-hi hì-lo-hi
	134470 134750	X54942 L29073	Hs.83758 Hs.1139	CDC28 protein kinase 2 cold shock domain protein A	hi-lo-hi
70	125819	AA044840	'Hs.251871	CTP synthase	hi-lo-hi
70	102993	BE262998	Hs.85137	cyclin A2	hi-lo-hi
	131185	BE280074	Hs.23960	cyclin B1	hi-lo-hi
	106350	AK001404	'Hs.194698	cyclin B2	hi-lo-hi
	103080	AU077231	Hs.82932	cyclin D1 (PRAD1: parathyroid adenomatos	hi-to-hi
75	101216	AA284166	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK	hi-lo-hi
	100589	AW247430	Hs 84152	cystalhionine-beta-synthase	hi-to-hi
	130655	AI831962	Hs.17409	cysteine-rich protein 1 (intestinal)	hi-to-hi
	101473	M22976	Hs.83834	cylochrome b-5	hi-lo-hi
	101468	BE538296	*Hs.181028	cylochrome c coidase subunit Va	hi-lo-hi
80	103546	Z14244	*Hs.75752	cytochrome c axidase subunit VItb	hi-lo-hi
	100829	AA471098	Hs.278544	acetyl-Coenzyme A acetyltransferase 2 (a	hi-lo-hi
	102469	AF058293	Hs.180015	D-dopachrome taulomerase	hi-lo-hi

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	114292	Al815395	Hs.184641	fatty acid desaturase 2	hi-lo-hi
	100656	BE250162	Hs.83765	dihydrofolale reductase	hi-lo-hi
	133799 129113	W24087 BE543205	Hs,76285 *Hs,288771	DKFZP554B167 protein	hi-lo-hi hi-lo-hi
5	332732	AF191019	Hs.8361	DKFZP586A0522 protein hypothetical protein, estradiol-induced	m-10-ni hi-lo-hi
,	108846	AL117452	*Hs.44155	DKFZP586G1517 protein	hi-lo-hi
	133903	X63692	*Hs.77462	DNA (cylosine-5-)-melhytransferase 1	hi-lo-hi
	320099	AW411307	Hs.114311	CDC45 (cell division cycle 45, S.cerevis	hi-lo-hi
	321960	AA723883	Hs.302446	hypothetical protein MGC10334	hi-lo-hi
10	324988	AK001379	"Hs.121028	hypothetical protein FLJ10549	hi-lo-hi
	303274	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	301804	AK001458	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
	300551	AW408800	Hs.104859	hypothetical protein DKFZp762E1312	hi-lo-hi
15	304541	AA482561	Hs.169476	glyceraldehyde-3-phosphate dehydrogenase	hi-lo-hi hi-lo-hi
13	129075	AA464716 BE250162	*Hs.83765	gb:zx82c11.s1 Soares overy ternor NbHOT H dihydrofolale reductase	hi-lo-hi
	111003	N52980	Hs.83765	ditydrofolale reductase	hi-lo-hi
	115536	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hì-lo-hi
	108857	AK001468	Hs.62180	anillin (Drosophila Scraps homolog), act	hi-lo-hi
20	332397	AB027249	Hs.104741	PDZ-binding kinase; T-cell originated pr	hi-lo-hi
	330714	AA263143	Hs.24596	RAD51-Interacting protein	hi-lo-hi
	104636	R82252	Hs.106106	Horno saplens cAMP-dependent protein kina	hi-lo-hi
	104986	AW088826	Hs.22971	ESTs	hi-lo-hi
25	105076	A)598252	Hs.37810	ESTs	hi-lo-hi
25	105312 105388	BE613348 AW575008	"Hs.23348 Hs.11355	S-phase kinase-associated protein 2 (p45	hi-lo-hi hi-lo-hi
	105953	BE410556	Hs.11305 Hs.236556	thymopoletin hypothetical protein STRAIT11499	hi-lo-hi
	106266	Al765107	"Hs.274422	hypothetical protein FLJ20550	hi-lo-hi
	106889	U46258	Hs.18349	HSPC145 protein	hi-lo-hi
30	109220	AV/958181	Hs.189998	ESTa	hi-lo-hi
	113158	AA328102	Ha.24641	cytoskeleton associated protein 2	hi-lo-hi
	114542	AW970128	"Hs.293380	ESTs	hi-io-hi
	114986	AK000361	Hs.133260	hypothetical protein FLJ20354	hi-lo-hi
2.0	115291	BE545072	'Hs.122579	hypothetical protein FLJ10461	hi-lo-hi
35	115414 115471	AA662240	Hs.283099 Hs.59346	AF15q14 prolein	hi-lo-hi hi-lo-hi
	115471	AK001376 BE614387	Hs.59346 Hs.47376	hypothetical protein FLJ10514 ESTs, Moderately similar to T50635 hypot	ni-io-ni hi-io-hi
	115652	BE093589	Hs.38178	hypothetical protein FLJ23468	hi-lo-hi
	116121	AK001330	Hs.48855	hypothetical protein FLJ 10458	hi-lo-hi
40	116130	AW183533	Hs38178	hypothetical protein FLJ23468	hi-lo-hi
	116448	BE268321	Hs.208912	hypothelical protein MGC861	hi-lo-hi
	116787	AW362955	Hs.15641	ESTa	hi-io-hi
	118336	BE327311	Hs.47166	HT021	hi-lo-hi
4.0	120649	AA687322	Hs.192843	leucine zipper protein FKSG14	hi-lo-hi
45	121503	AA412049	Hs.290347	ESTs	hi-lo-hi
	121748 122860	BE536911 AA464414	Hs.234545	Homo sapiens NUF2R mRNA, complete cds gb:zx78g01.s1 Soares ovary tumor NbHOT H	hi-lo-hi hi-lo-hi
	123477	AF217515	Hs.283532	uncharacterized bone marrow protein BM03	hi-lo-hi
	130338	Al375726	"Hs.279918	hypothetical protein	hi-lo-hi
50	130580	BE567313	Hs.183109	mongamine oxidase A	hi-lo-hi
	131148	AW963675	"Hs.303125	p53-induced protein PIGPC1	hi-lo-hi
	131826	BE514605	"Hs.289092	Homo saplens cDNA: FLJ22380 fis, clone H	hl-lo-hi
	131937	AI907735	Hs.21446	Homo sapiens mRNA for KIAA1716 protein,	hi-lo-hi
	131965	W79263	Hs.35962	ESTs	hi-lo-hi
55	132371	AA235448	Hs.46677	PRC2000 prolein	hi-lo-hi hi-lo-hi
	133626 300942	AW836130 AW301344	Hs.75277 Hs.122908	hypothetical protein FLJ13910 Homo sapiens, clone IMAGE:3048353, mRNA,	ni-io-ni hi-io-hi
	300953	AW301399 AA542845	Hs.122908 Hs.294088	ESTs	hi-lo-hi
	302656	BE090580	Hs.70704	Homo sapiens, clone IMAGE:2823731, mRNA,	hi-lo-hi
60	311928	T62216	Hs.270840	FSTs	hi-lo-hi
	313637	AK000742	Hs.126774	L2DTL protein	hi-lo-hi
	313832	AW271106	Hs.133294	ESTs .	hi-lo-hi
	316465	AW574774	Hs.121692	ESTs	hi-lo-hi
	317202	AA894880	Hs.181181	ESTs	hi-lo-hi
65	320771	R74441	Hs.117176	poly(A)-binding protein, nuclear 1	ht-lo-hi
	321636	AJ820961	Hs.193465	ESTs	hi-lo-hi hi-lo-hi
	330867 331442	AW978991 H77381	Hs.221197 Hs.159420	ESTs ESTs	hi-lo-hi
	106654	AW075485	Hs.286049	phosphoserine aminotransferase	hi-lo-hi
70	106590	Al350260	Hs.301539	hypothetical protein MGC2633	hi-lo-hi
, ,	128460	T16206	Hs.237164	ESTs, Highly similar to LDHH_HUMAN L-LA	hì-lo-hi
	114394	T34462	Hs.103291	neuritin	hi-lo-hi
	315936	AW069807	Hs.271252	ESTs	hi-lo-hi
-	108886	AW248434	Hs.91521	hypothetical protein	hi-lo-hi
75	129241	A1878857	Ha.109706	hemalological and neurological expressed	hi-lo-hi
	104978	Al199268	Hs.19322	ESTs, Weakly similar to CGHU7L collagen	hi-lo-hi hi-lo-hi
	129626 118895	F13272 BE304917	Hs.111334 Hs.31097	ferritin, light polypeptide hypothetical protein FLJ21478	ni-io-ni hi-lo-hi
	332577	A/826268	Hs.27789	ESTs, Weakly similar to MCAT_HUMAN MITOC	hi-io-hi
80	116732	AW152225	Hs.165909	FSTs	hi-lo-hi
00	106774	AI216748	Hs.14587	ESTs, Weakly similar to AF151859 1 CGI-1	hi-lo-hi
	108818	BE612676	Hs.303116	stromal cell-derived factor 2-like 1	hi-lo-hi

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	315618	Al287341	"Hs.154029	bHLH factor Hes4	hi-lo-hi
	110561	AA379597	Hs.5199	HSPC150 protein similar to ubiquitin-con	hi-to-hi
	132959 103195	AW014195 AA351647	Hs.61472 Hs 2642	ESTs, Weakly similar to unknown [S.cerev	hi-lo-hi ht-lo-ht
5	100368	PA35164/	Hs.2642 Hs.153479	eukanyolic translation elongation factor	nt-to-nt hi-lo-hi
,	103177	BE244377	'Hs.48876	extra spindle poles, S. cerevisiae, homo famesyl-ciphosphale famesyltransferase	hi-lo-hi
	109141	AF174600	Hs.193380	F-box protein Fbx20	hi-ko-hi
	100676	X02761	*Hs.287820	fibronectin 1	hi-lo-hi
	100254	AA452181	Hs.77643	FK506-binding protein 1B (12.6 kD)	hi-lo-hi
10	133688	U71321	Hs.7557	FK506-binding protein 5	hi-lo-ht
	107129	AC004770	'Hs.4756	flap structure-specific endonuclease 1	hi-lo-hi
	102696	BE540274	Hs.239	forkhead box M1	hi-lo-hi
	101753	L11144	Hs.1907	galarin	hi-lo-hi
15	101597	AA317089	'Hs.597	glutamic-oxaloacelic transaminase 1, sol	hi-lo-hi
13	133512 130080	L18861 X14850	Hs.147097	gb:Human Goti-mbp gene, exon 1,	hi-lo-hi hi-lo-hi
	101600	BE561617	'Hs.119192	H2A histone family, member X H2A histone family, member Z	hi-lo-hi
	101332	J04088	*Hs.156346	lopoisomerase (DNA) II alpha (170kD)	hi-lo-hi
	132967	AA316181	Hs.61635	six transmembrane epithelial anligen of	hi-lo-hi
20	129726	H15474	Hs.132898	falty acid desalurase 1	hi-lo-hi
	106925	AK002011	Hs.37558	hypothetical prolein FLJ11149	hi-lo-hi
	105643	BE621719	Hs.173802	KIAA0603 gene product	hi-lo-hi
	116028	H59799	Hs.42644	thioredoxin-like	hi-lo-hi
25	105437	AF151076	Hs.25199	hypothotical prolein	hi-lo-hi
23	122512	AF053305	Hs.98658	budding urinhibited by benzimidazoles 1	hi-lo-hi
	131991 135015	AF053306 AW361638	Hs.36708 Hs.278338	budding urinhibited by benzimidazoles 1 LGN protein	hi-lo-hi hi-lo-hi
	102208		HS.276336	glo:Human mRNA clone with similarity to L	ni-to-ni hi-lo-hi
	102208	U22961 AL119964	Hs.75616	go:Human mikiya cione wiin similaniy to L seladin-1	ni-to-ni hi-lo-hi
30	100447	NM 014767	Hs.74583	KIAA0275 gene product	hi-lo-hi
50	116578	D21262	Hs.75337	nucloolar phosphoprolein p130	hi-lo-hi
	130350	AA369601	Hs.239138	pre-B-cell colony-enhancing factor	hi-lo-hi
	101045	J05614		qb:Humen proliferating cell nuclear anti	N-lo-hi
	101544	M31169		gb:Humen propionyl-CoA carboxylese beta-	hi-lo-hi
35	113674	NM_014214	Hs.5753	inositol(myo)-1(or 4)-monophosphatase 2	hi-lo-hi
	102260	AL039104	Hs.159557	karyopherin alpha 2 (RAG cohort 1, impor	hi-lo-hi
	100154	H60720	Hs.81892	KIAA0101 gene product	hi-lo-hi
	100199	BE562298	Hs.71827	K/AA0112 protein; homolog of yeast ribos	hi-lo-hi
40	100372	NM_014791	Hs.184339	KIAA0175 gene product	hi-lo-hi hi-lo-hi
40	131514	D83777 BE270734	"Hs.75137 "Hs.2795	K/AA0193 gene product Isolate dehydrogensse A	hi-lo-hi
	102938	W27518	Hs.234489	laciale deliyorogenase B	hi-lo-hi
	105811	BE617695	Hs.286192	protein phosphatase 1, regulatory (inhib	hi-lo-hi
	101013	BE300094	*Hs.227751	lectin, gatacioside-binding, soluble, 1	hi-lo-hi
45	124148	BE300094	"Hs.227751	lectin, galactoside-binding, soluble, 1	hi-lo-hi
	102968	AU076611	Hs.154672	methylene tetrahydrofolate dehydrogenase	hi-lo-hi
	130149	AW067805	Hs.172665	methyleneteirahydrofolate dehydrogenase	hi-lo-hi
	114767	A)859865	Hs.154443	minichromosome maintenance deficient (S.	hi-lo-hi
50	129168	A)132988	Hs.109052	chromosome 14 open reading frame 2	hi-lo-hi
30	105011	BE091926 AW500470	Hs.16244 Hs.117950	mitotic spindle colled-coll related prot multifunctional polypeplide similar to S	hi-lo-hi hi-lo-hi
	102808	BE242818	"Hs.179606	nuclear RNA helicase, DECD variant of DE	hi-lo-hi
	318617	AW247252	Hs.75514	nucleoside phosphorylase	hi-lo-hi
	101568	M81740	Hs.75212	omithine decarboxytase 1	hi-lo-hi
55	102076	BE299197	Hs.179665	cyclin-dependent kinase inhibitor 1A (p2	hi-lo-hi
	100202	BE294407	'Hs.99910	phosphofructokinase, platelet	hi-lo-hi
	101032	BE206854	Hs.46039	phosphoglycerate mutase 2 (muscle)	hi-lo-hi
	130553	AF062649	"Hs.252587	pituilary tumor-transforming 1	hi-lo-hi
60	101626	M57399	Hs.44	pleiotrophin (heparin binding growth fac	hi-lo-hi
60	101992	X90725	Hs.77597 Hs.41270	polo (Drosophie)-like kinase procollagen-lysine, 2-oxoglutarate 5-dio	hi-lo-hi hl-lo-hi
	132184 101396	AI752235 BE267931	'Hs.78996	protiferating cell nuclear antigen	hi-lo-hi
	119018	AA631143	Hs.179809	ESTs	hi-lo-hi
	101840	AA236291	Hs.183583	serine (or cysteine) proleinase inhibito	hi-lo-hi
65	332640	BE568452	Hs.5101	protein regulator of cytokinesis 1	hi-lo-hi
	132543	BE568452	Hs.5101	protein regulator of cytokinesis 1	hi-lo-hi
	101118	AA371931	"Hs.77422	proteolipid protein 2 (colonic epithellu	hi-lo-hi
	109166	AA219691	Hs.73625	RAB6 interacting, kinesin-like (rabkines	hi-lo-hi
	100630	AC004770	'Hs.4756	flap structure-specific endonuclease 1	hi-lo-hi
70	107059	BE614410	Hs.23044	RAD51 (S. cerevisiae) homolog (E colli Re	hi-lo-hi
	321693	AA227069	Hs.173737	ras-related C3 botulinum toxin substrate	hi-lo-hi
	101148	NM_002923	Hs.78944	regulator of G-protein signalling 2, 24k	hi-lo-hi
	130567 103076	AA383092 NM 001034	Hs.1608	replication protein A3 (14kD)	hi-lo-hi hi-lo-hi
75	103076	NM_001034 BE536069	Hs.75319 Hs.2962	ribonucleolide reductase M2 polypeptide S100 calcium-binding protein P	ni-to-ni hi-lo-hi
, ,	102212	AW411491	Hs.75069	serine hydroxymethytransferase 2 (mitoc	hi-lo-hi
	104254	AW411425	Hs.180655	segne/hreggine kingse 12	hì-lo-hi
	102748	BE018138	Hs.24447	sigma receptor (SR31747 binding protein	hi-lo-hi
	102012	BE259035	Hs.118400	singed (Drosophila)-like (sea urchin fas	hì-lo-hi
80	102522	BE250944	Hs.183556	solute carrier family 1 (neutral amino a	hi-lo-hi
	132994	AA112748	Hs.279905	clone HQ0310 PR00310p1	hì-lo-hì
	101971	Z49105	"Hs. 289105	synovial sercoma, X breakpoint 2	hi-lo-hi

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126645 AA316181 Hs.61635 six transmembrane epithelial antigen of hi-lo-hi 103058 X57348 Hs.184510 hi lo hi 102632 1366618 Hs 250581 SWUSNF related, matrix associated, acti hi.lo.hi "Hs.289105 synovial sarcoma, X breakpoint 2 programmed cell death 5 thymidylate synthetase hì-lo-hi 103269 AF230962 5 AA622037 Hs 166468 hi-lo-hi 128920 100114 X02308 Hs.82962 hì-lo-hi 102846 BE264974 Hs.6566 thyroid hormone receptor interactor 13 hì-lo-h 131877 JOANSE *Hs.156346 topoisomerase (DNA) II alpha (170kD) hi lo hi 100866 1114134 Hs.75113 general transcription factor IIIA hi-lo-hi 10 hì-lo-hì 133893 A1434699 Hs 77356 transferrin receptor (p90, CD71) hì-lo-hì 130135 44311426 "Hs 21635 tubulin, gamma 1 AA479005 Hs.154036 tumor suppressing subtransferable candid ubiquinol-cylochrome c reductase, Rieska hi-lo-hi 130287 126180 L32977 Hs.3712 hi-lo-hi 101536 NM_006002 Hs.77917 ubiquitin carboxyl-terminal esterase L3 ubiquitin carrier protein E2-C zinc linger protein 145 (Kruppel-like, e hi-lo-hi 15 102687 NM_007019 "Hs.93002 hi-lo-hi 103556 Z19002 Hs 37096 hì-lo-hi-k 300022 AJ002744 Hs.246315 UDP-N-acetyl-alpha-D-galactosamine:polyp Hs.11806 7-dehydrocholesterol reductase hi-to-hi-to 133015 129642 NM_001360 Hs.11806 hì-lo-lo 20 134369 AF207664 Hs.8230 a disinlegin-like and metalloprolesse'(hi-lo-lo 300023 hi-lo-lo 125183 AV660804 Hs.301417 AHNAK nucleoprotein (desmoyokin) "Hs.301417 AHNAK nucleoprotein (desmoyokin) hi-lo-lo hi-lo-lo 101766 Leanago BE265133 "Hs.217493 hi-lo-lo hi-lo-lo 133516 annexin A2 25 ATPase, Na+/K+ Iransporting, beta 1 poly 102146 AW162057 He 78629 Homo sapiens clone 24651 mRNA sequence Hs.74034 hi-lo-lo 318538 A1750979 103554 Al878826 Hs.323469 caveolin 1, caveolae prolein, 22kD hi-lo-lo CH.X_hs gli5868838 CH22_FGENES.369_12 hi-lo-lo 328365 334282 hHo-lo 30 CH22_FGENES.452_5 hl-lo-lo 334901 CH22_FGENES.499_5 hi-lo-lo hi-lo-lo 3351/0 335682 CH22_FGENES.595_2 335756 CH22_FGENES.604_5 hi-lo-lo 303951 AW475081 Hs.172928 collagen, type I, alpha 1 collagen, type V, alpha 2 DKFZP586M1523 protein hi-lo-lo hi-lo-lo 35 134421 AU077198 Hs 82985 hì-lo-lo 131101 BE387581 He 22981 41)077333 "He 160483 erythrocyte membrane protein band 7.2 (s hi-lo-lo 124153 AU077333 "Hs.160483 erythrocyte membrane protein band 7.2 (s 103338 AL137517 "Hs.306201 hypothetical protein DKFZp564O1278 hi-lo-lo 322035 40 H84730 Hs.326391 ESTs, Highly similar to KIAA1437 protein hi-io-lo 301872 AB037858 Hs.173484 hypothelical protein FLJ10337 hi-lo-lo 303820 hypothekcal prolein FLJ10337 gb:yb96h03.s1 Stratagene iung (937210) H gb.mm75h11.s1 NCL_CGAP_Co9 Home sapiens EST, Weakly similar to zinc finger prot hi-lo-lo 304040 T58155 44576453 hi-lo-lo hi-lo-lo 304735 Hs.308058 300000 A1138828 45 AW368576 Hs.139851 caveolin 2 hi-lo-lo 128789 132057 AB037858 He 173484 hypothetical protein FLJ10337 hi-lo-lo 114795 AB037858 Hs.173484 hypothetical protein FLJ10337 hi-lo-lo hypothetical protein FLJ10829 cyloskeleton associated protein 2 hi-lo-lo 104204 AX001691 He 57655 AA328102 He 24841 hi-lo-lo 105200 50 AL047588 Hs.10283 RNA binding motif protein 8B hi-lo-lo 105493 Al188161 Hs.144627 ESTs hi-lo-lo 107977 AA766605 "Hs,47099 hypothetical protein FLJ21212 hi-lo-lo 108880 AL109729 Hs.18948 ESTs, Highly similar to A31026 probable hi-lo-lo 111157 RE150305 He 87089 hl-lo-lo 116202 FSTe. 55 hi-lo-lo hi-lo-lo 120689 AW134519 Hs 96125 **ESTe** cartilage linking protein 1 121947 AA449828 He 2700 A1637471 He 107801 ESTS hi-lo-lo 124192 BE395085 Hs.10086 type I transmembrane protein Fn14 hi-lo-lo 128515 W19744 Hs.180059 Homo saciens cDNA FLJ20653 fls, clone KA hi-lo-lo 130466 60 131076 AA749230 Hs.22666 FSTe hl-lo-lo apelin; peptide ligand for APJ receptor ESTs 131084 NM_017413 Hs.303084 hi-to-to hi-lo-lo hi-lo-lo 134109 44349031 Hs.7913 Al478933 Hs.188260 ESTs 300258 302767 H94900 Hs.17882 ESTs hì-lo-lo 65 R43707 ESTs, Weakly similar to PIHUSD salivary hi-lo-lo 312301 He 133159 312689 AW450461 Hs.203965 ESTS hi-lo-lo AI284219 hi-lo-lo hi-lo-lo 315715 Hs.130749 ESTs A4679430 ESTs 315843 Hs 191897 322447 Al735759 Hs 52620 integrin, beta 8 hi-lo-lo 70 322826 AI807883 Hs.201771 ESTs hi-lo-lo 324867 Al624707 "He 5921 Homo sapiens cDNA: FLJ21592 fis, clone C hl-lo-lo 331336 AA287450 Hs.93842 Home sepiens cDNA: FLJ22554 fis, clone hi-lo-lo 331353 AA953006 Hs.88143 **ESTs** hi-lo-lo A1654133 Bryrold receptor interacting protein 15 ESTs, Moderately similar to PT0375 natur hi-lo-lo 133063 He 30212 75 BE567130 He 311389 hi-lo-lo 311036 BE546947 Hs.44276 homeo box C10 hi-lo-lo 108647 homeo box C10 hypothetical protein FLJ22622 hypothetical protein FLJ22041 similar to ESTs, Weakly similar to Y161_HUMAN HYPOT ESTs, Weakly similar to T17330 hypotheti 124955 AA376768 'Hs.324841 AW953484 Hs.3849 hi-lo-lo 113923 310557 AI431798 He 164192 hi-lo-lo hi-lo-lo 80 Hs 127812 302043 AJ581344 X02761 Hs.287820 hi-lo-lo 128453 fibronecin 1 305232 AA670052 Hs.169476 glyceraldehyde-3-phosphale dehydrogenase

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	117642	U55184	'Hs.154145	hypothetical protein FLJ11585	hi-lo-lo
	115881	NM_005756	Hs.184942	G protein-coupled receptor 64	hi-lo-lo
	133666 103262	U56725 X78565	Hs.75452 Hs.289114	heal shock 70kD protein 2 hexabraction (tenascin C, cytotactin)	hi-lo-lo hl-lo-lo
5	100793	S69027	119.203114	gb:HOX C6=class I homeodomain (fragment	hi-lo-lo
-	102289	U32114		\$	hi-lo-lo
	319109	Z45662	Hs.90797	Homo sapiens clone 23620 mRNA sequence	hi-lo-lo
	116357	AF052107	Hs.90797	Homo sapiens clone 23620 mRNA sequence	hi-lo-lo
10	101497 105508	W05150 AA173942	"Hs.37034 Hs.326416	homeo box A5 Homo sapiens mRNA; cDNA DKFZp564H1916 (f	hi-lo-lo hi-lo-lo
10	302290	AA179949	Hs.175563	Homo sapiens mRNA; cDNA DKFZp564N0763 (f	hi-lo-lo
	102838	R34657	Hs.80658	uncoupling protein 2 (milochondrial, pro	hì-lo-lo
	100235	D29954	Hs.13421	KIAA0056 protein	hi-lo-lo
1.5	133507	NM_002206	Hs.74369	integrin, alpha 7	hi-lo-lo
15	125573 103059	AJ351642 X57351	Hs.182241 Hs.174195	interferon induced transmembrane protein interferon induced transmembrane protein	hì-lo-lo hì-lo-lo
	330415	D83777	"Hs.75137	KIAA0193 gene product	hi-lo-lo
	303054	BE265848	Hs.289080	colon cancer-associated protein Mic1	hì-lo-lo
	133579	X75346	Hs.75074	mitogen-activated protein kinase-actival	hl-lo-lo
20	100528	BE386801	Hs.21858	trinucleotide repeat containing 3	hi-lo-lo
	107480 133050	AF001691 X73424	Hs.74304	periplakin	hi-lo-lo hi-lo-lo
	133060	X73424 AJ186431	Hs.63788 Hs.296638	propionyl Coenzyme A carboxylase, bela p prostate differentiation factor	hl-lo-lo
	106390	AJ297436	Hs.20166	prostate stem cell antigen	hi-lo-lo
25	302124	AA676403	Hs.145078	regulator of differentiation (in S. pomb	hì-lo-lo
	129823	X00949	'Hs.105314	relaxin 1 (H1)	hl-lo-lo
	134444	BE184455	"Hs.251754	secretory leukocyte prolesse Inhibitor (hi-lo-lo hi-lo-lo
	103240 115761	UB1961 AA366037	Hs.2794 Hs.90911	sodium channel, nonvollage-galed 1 alpha solute carrier family 16 (monocarboxylic	ni-lo-lo hi-lo-lo
30	321412	AA300037 AI674383	Hs.22891	solute carrier family 7 (cationic amino	hi-lo-lo
20	126487	AA283809	Hs. 184801	solute carrier family 7 (cetionic amino	hl-lo-lo
	101759	M80244	Hs.184601	solute carrier family 7 (cationic amino	hi-lo-lo
	112941	AW163034	Hs.6467	synaplogyrin 3	hl-lo-lo
35	134351 125924	BE272506 BE272506	"Hs.82109 "Hs.82109	syndecan 1 syndecan 7	hi-lo-lo hi-lo-lo
33	120024	AA033627	Hs.21858	trinucleotide repeal containing 3	hi-lo-lo
	133473	AW301993	Hs.73980	troponin T1, skeletal, slow	hi-lo-lo
	101042	T46839	*Hs.10319	UDP glycosyltransferase 2 family, polype	hl-lo-lo
40	129565	X77777	Hs.198726	vasoactive intestinal peptide receptor 1	hi-lo-lo
40	102992 106968	M95430 BE185536	'Hs.155191 Hs.300816	villin 2 (ezrin) Homo saplens mRNA; cDNA DKFZp554I172 (fr	hHo-lo lo-hi lo
	132618	AL050025	'Hs.279916	hypothetical protein FLJ20151	lo-hi-hi
	100187	D17793	'Hs.78183	eldo-kelo reductase family 1, member C3	lo-hi-hi
	116334	AL038450	Hs.48948	ATP2C1 calcium transport ATPase, same as	lo-hi-hi
45	134454	NM_013230	Hs.286124	CD24 antigen (small cell lung carcinoma	lo-hl-hi
	302067 105500	BE542706 AW602166	Hs.222399 Hs.222399	CEGP1 protein CEGP1 protein	lo-hì-hì lo-hì-hì
	100500	AA557660	'Hs.76152	decorin	io-hi-hi
	129285	AA530892	Hs.171695	dual specificity phosphalase 1	lo-hi-hi
50	117789	N48294	Hs.46850	EST	lo-hi-hi
	330786	BE379594	'Hs,49136	ESTs, Moderately similar to ALU7_HUMAN A	lo-hi-hi
	319808 303502	T58960 BE174240	Hs.17283	hypothelical prolein FLJ10590 gb:QV1-HT0573-290200-092-406 HT0573 Homo	lo-hi-hi lo-hi-hi
	116780	H22566	'Hs,30098	ESTs	lo-hl-hi
55	104189	AB040927	Hs.301804	KIAA1494 protein	lo-hi-hi
	105588	L43821	Hs.80261	enhancer of filamentation 1 (cas-like do	lo-hi-hi
	105731	AA834864	Hs.29131	nuclear receptor coactivator 2	lo-hl-hl
	105772	H57111	Hs.221132	ESTs	io-hi-hi io-hi-hi
60	105794 113098	H24530 N77737	Hs.273294 Hs.8349	hypothetical protein FLJ20069 Apobec-1 complementation factor: APCBEC-	lo-hi-hi
00	113803	AW880709	*Hs.283683	chromosome 8 open reading frame 4	lo-hl-hi
	114530	AA601038	Hs.191797	ESTs	lo-hi-hi
	116188	AA468183	Hs.184598	Homo sapiens cDNA: FLJ23241 fis, clone C	lo-hi-hi
65	117330	AI904095	Hs.43423	ESTs	lo-hi-hi lo-hi-hi
03	117701	BE063921 Al189754	Hs.295971 Hs.144330	ESTs FSTs	lo-hi-hi
	124083	AW195237	Hs.7734	hypothetical protein FLJ22174	lo-hi-ht
	124690	AW883529	Hs.173830	ESTs	lo-hi-hi
70	130798	AA068809	Hs.19525	hypothetical protein FLJ22794	lo-hi-hi
70	131524	AB040927 AW960474	Hs.301804	KIAA1494 protein ESTs	lo-hì-hi lo-hì-hi
	132116	AW970859	Hs.40289 Hs.313503	ESTS	lo-hi-hi
	310219	AI221087	Hs.147761	ESTs	lo-hi-hi
	310598	Al439136	Hs.140546	ESTs	lo-hi-hi
75	310884	AW014684	Hs.232189	ESTs	lo-hi-hi
	311587 312240	AJ828254 R36475	Hs.271019 Hs.24321	ESTs, Weakly similar to SMN1_HUMAN SURVI Homo sapiens cDNA FLJ12028 fils, clone HE	lo-hi-hi lo-hi-hi
	312240	R36475 AA677934	Hs.117864	ESTs	lo-ni-ni lo-hi-hi
	314219	AA262331	Hs.48376	Homo sapiens clone HB-2 mRNA sequence	lo-hi-hi
80	315052	AA876910	Hs.134427	ESTs	lo-hi-hi
	331919	AA446369	Hs.119316	ESTs	lo-hì-hì
	133240	AK001489	Hs.242894	ADP-ribosylation factor-like 1	lo-hi-hi
				400	

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	134006	Z45957	Hs.7837	G-protein-coupled receptor induced prote	lo-hi-hi
	124847 129087	W07701 Al348027	"Hs.304177 Hs.108557	Homo sapiens clone FLB8503 PRO2286 mRNA, Homo sapiens clone PP1057 unknown mRNA	lo-hi-hi lo-hi-hi
	131762	AA744902	'Hs.107767	hypothetical protein PRO1489	lo-hl-hi
5	129000	AA744902	*Hs.107767	hypothetical protein PRO1489	lo-hì-hì
	105713	Al122843 N66845	"Hs.184319	ESTs, Weakly similar to KIAA 1006 protein gbzza46c11.s1 Soares fetal liver spicen	ko-hi-hi ko-hi-hi
	118381	N64513	Hs.48994	ESTs, Wealthy similar to AF151800 1 CGI-4	lo-hi-hi
10	105057	AA134233		gb:zo20f10.s1 Stratagene colon (937204)	lo-hi-hi
10	131507 124970	A)826268 DE272862	Hs.27769 Hs.106534	ESTs, Wealdy similar to MCAT_HUMAN MITOC hypothetical protein FLJ22625	lo-hí-hì lo-hì-hì
	130094	NM 001471	'Hs.167017	gamma-aminobetyric acid (GABA) B recepto	lo-hi-hi
	302357	X03178	Hs.198246	group-specific component (Vitamin D bind	lo-hì-hì
15	113231 111923	AA278583 BE383234	Hs. 180737 Hs. 25925	Homo sapiens clone 23664 and 23905 mRNA Homo sapiens clone 23860 mRNA sequence	lo-hì-hì lo-hì-hì
13	128530	Al932995	Hs.183475	Homo espiens clone 25061 mRNA sequence	lo-hi-hi
	128987	Al339046	Hs.107637	hypothetical prolein FLJ12806	lo-hi-hi
	315368 133944	AB037745 AW068579	Hs.104696 Hs.7780	KIAA1324 protein Homo sapiens mRNA; cDNA DKFZp564A072 (fr	lo-hi-hi lo-hi-hi
20	115084	BE383668	'Hs.42484	hypothetical prolein FLJ10618	lo-hì-hì
	132883	AA373314	Hs.5897	Homo saplens mRNA; cDNA DKFZp586P1822 (f	lo-hi-hi
	109623 130577	AW207385 M69241	Hs.295901 *Hs.162	KIAAM93 protein insulin-like growth factor binding prote	lo-hì-hì lo-hì-hì
	101889	AF188747	"Hs.181350	kallikrein 2, prostatio	lo-hl-hl
25	130336	AA535210	'Hs.171995	kallikrein 3, (prostate specific antigen	lo-hì-hì
	128180 134921	AW949068 AL137491	Hs.171995 Hs.125511	kallikrein 3, (prostate specific antigen Homo sapiens mRNA; cDNA DKFZp434P1530 (f	lo-hi-hi lo-hi-hi
	302385	AJ224172	Hs.204096	lipophilin B (utercelobin family member)	lo-hì-hi
30	117921	AA021459	Hs.306480	Homo sapiens mRNA; cDNA DKFZp761E2112 (f	lo-hi-hi
30	101701 130356	NM_002436 AF127577	Hs.1861 Hs.155017	membrane prolein, palmitoylated 1 (55kD) nuclear receptor interacting protein 1	lo-hi-hi lo-hi-hi
	101763	AB001914	Hs.170414	paired basic amino acid cleaving system	lo-hi-hi
	130342	U81802	Hs.154846	phosphatidylinositol 4-kinase, catalytic	lo-hi-hi
35	130760 101481	AW379130 N98589	Hs.18953 Hs.76422	phosphodiesterase 9A phospholipase A2, group IIA (platelels,	lo-hi-hi lo-hi-hi
-	134032	NM_005025	Hs.78589	sarina (or cyslaina) prolainasa inhibito	lo-hi-hi
	303762	AF034799	Hs,30681 Hs,306480	protein tyrosine phosphalase, receptor I	lo-hi-hi lo-hi-hi
	110932	AA021459 U83993	Hs.306480 Hs.321709	Homo saplens mRNA; cDNA DKFZp761E2112 (f perinergic receptor P2X, ligand-cated to	lo-m-m lo-hi-hi
40	133886	U97276	Hs.77266	gulescin Q6	lo-hi-hi
	134142	BE244053	Hs.79362	retinoblastome-like 2 (p130)	lo-hi-hi
	100877	X80821 AU077115	Hs.302177 Hs.201675	H.sepiens mRNA for ribosomal protein L18 RNA binding motif protein 5	lo-hl-hi lo-hl-hi
	133011	NM_006379	Hs.171921	sema domain, immunoglobu'in domain (ig),	lo-hì-hì
45	132160	W26406 X62822	Hs.295923	seven in absentia (Drosophila) homolog 1	lo-hi-hi
	103110 130173	U38847	Hs.2554 Hs.151518	sialyltransferase 1 (bela-galactoside al TAR (HIV) RNA-binding protein 1	lo-hi-hi lo-hi-hi
	127435	X69086	"Hs.286161	TAR (HIV) RNA-binding protein 1 Homo septens oDNA FLJ13613 fis, clone PL	lo-hi-hl
50	110520 114660	N54069 AA071383	Hs.4082	lectin, galactoside-binding, soluble, 8 gb:zm61d05.r1 Stratagene fibroblast (937	lo-hi-hi lo-hi-hi
50	330541	NM_002038	Hs.265827	interferon, alpha-Inducible protein (clo	lo-hi-lo
	101488	AA508324	Hs.1852	acid phosphalase, prostate	lo-hi-lo
	332386 100569	NM_000481 AA535210	Hs.102 "Hs.171995	aminomethyltransferase (glycine cleavage	lo-hi-lo lo-hi-lo
55	134738	AU076801	Hs.89438	kalikrein 3, (prostate specific antigen cacherin 17, L1 cadherin (Iver-intestin	lo-hi-lo
	103119	X63629	Hs.2877	cadharin 3, typa 1, P-cadherin (placanta	lo-hl-lo
	302892 105402	AW176909 AB014680	Hs.42346 Hs.8786	calcineum-binding prolein catsarcin-1 carbohydrate (chondrollin 6/keratan) sul	lo-hi-lo lo-hi-lo
	102976	AU077174	"Hs.288181	calheosin H	lo-hi-lo
60	101793	W01076	"Hs.119663	CD59 antigen p18-20 (antigen identified	lo-hi-io
	129890 328164	Al868872	"Hs.282804	Home sapiens cDNA: FLJ22704 fis, clone H CH.06_hs gij5868068	lo-hi-lo lo-hi-lo
	328648			CH.07_hs qij5004473	lo-hi-lo
65	330032			CH.16_p2 gi[6682596	lo-hi-lo
65	330033 326816			CH.16_p2 glj6682596 CH.20_hs glj6552458	lo-hi-lo lo-hi-lo
	337603			CH22_C20H12.GENSCAN.16-2	lo-hi-lo
	338561			CH22_EM-AC005500.GENSCAN.421-5	lo-hi-lo
70	338562 333743			CH22_EM:AC005500.GENSCAN,421-6 CH22_FGENES.264_1	lo-hi-io lo-hi-io
,,,	333845			CH22 FGENES,290 3	lo-hi-lo
	333849			CH22_FGENES.290_8	lo-hi-io
	334221 334222			CH22_FGENES.360_1 CH22_FGENES.360_3	lo-hi-lo lo-hi-lo
75	334578			CH22_FGENES.406_1	lo-hi-lo
	336662			CH22_FGENES.41-1	lo-hì-lo
	336684 335289			CH22_FGENES.46-1 CH22_FGENES.527_2	lo-hi-lo lo-hi-lo
	335290			CH22_FGENES.527_3	lo-hi-lo
80	335293			CH22_FGENES.527_6	lo-hi-lo lo-hi-lo
	337182 335809			CH22_FGENES.570-2 CH22_FGENES.617_6 (same as BFH4)	lo-hi-lo
	333009			Committee of the commit	~10

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	335810			CH22_FGENES.617_7	b-hi-lo
	335824			CH22_FGENES.619_11 (same as BFH5)	lo-hi-lo
	336054			CH22_FGENES.683_3	lo-hi-lo
	333124			CH22_FGENES.81_8	lo-hi-lo
5	332340	AP000692	Hs.129781	chromosome 21 open reading frame 5	lo-hi-lo
-	130380	AI949359	Hs.143600	type I! Golgi membrane protein	lo-hi-lo
	102962	R50032	Hs.159263	collagen, type VI, alpha 2	lo-hi-lo
	331306	AF102546	Hs.63931	dachshund (Crosophila) homolog	lo-hi-lo
	319408	AA448090	Hs.87359	ESTs, Highly similar to RB18 MOUSE RAS-R	ko-hi-lo
10	312197	T96203	110.01000	gb:ye48b07.r1 Soares fetal liver spleen	lo-hi-lo
	312405	A1523875		gb:lg97d04.x1 NCI_CGAP_CLI.1 Homo sapiens	lo-hi-lo
	312939	AA495930	Hs 24444	Homo sapiens cDNA: FLJ22165 fis, clone H	lo-hi-lo
	313475	AA010200	Hs.175551	ESTs	lo-hi-lo
	313624	AA525775	Hs.292523	ESTs	b-hi-lo
15	316897	AA838114	Hs.292523	ESTs	lo-hi-lo
13	317850				lo-hi-lo
	318541	A1681545 T30290	Hs.152982 Hs.107515	hypothetical protein FLJ13117 ESTs	lo-hi-lo
	321325 321696	AB033100	Hs.300646 Hs.76228	KIAA protein (similar to mouse paladin)	lo-hi-lo lo-hi-lo
20		AA628791	HS.76228	amplified in osteosarcoma	
20	322189	H65014	11 /0-00	gb:yu86f10.r1 Weizmann Olfactory Epithel	lo-hi-lo
	322463	Al242754	Hs.137306	ESTs	lo-hi-lo
	322540	R76593		gb:y/60c11.r1 Soares placenta Nb2HP Homo	lo-hi-lo
	323131	AK002088	Hs.270124	Homo sapiens cDNA FLJ11226 fis, clone PL	lo-hi-lo
25	323243	W47525	Hs.110771	Homo sapiens cDNA: FLJ21904 fis, clone H	lo-hi-lo
25	323591	AA301270		gb:EST14192 Testis tumor Homosapiens cD	lo-hi-lo
	323753	AK002161	Hs.70266	yeast Sec31p homolog	lo-hi-lo
	323835	AL042005	Hs.1117	tripeplidyl peplidase II	lo-hi-lo
	323926	AA354572		gb:EST62857 Junkat T-cells V Homo saplen	lo-hì-lo
	324047	A1433357	"Hs.271340	ESTs	lo-hi-lo
30	324330	AA884766		gb:am20a10.s1 Soares_NFL_T_GBC_S1 Homo s	lo-hi-lo
	324753	AA612626	Hs.144871	Homo saplens cDNA FLJ13752 fis, clone PL	lo-hi-lo
	300702	AA075481	Hs.111334	familie linkt nakmanlida	lo-hi-lo
	301712	BE083080	Hs.274323	Homo sapiens, Similar to sialytransfera KIAA0853 protein	lo-hi-lo
	302380	AA325633	Hs.136102	KIAA0853 protein	lo-hi-lo
35	302970	W05608	Hs.312679	EST	lo-hi-lo
	303187	AA115962	Hs.323423	ESTs, Moderately similar to B Chain B,	lo-hi-lo
	303194	AA082000		ob:zn26f07.r1 Stratagene neuroepithelium	lo-hl-lo
	305812	AA782347	Hs.272572	hemoglobin, alpha 2	lo-hi-lo
	304263	AA062837		gb:zm05b11.s1 Stratagene corneal stroma	lo-hi-lo
40	304275	AA070605		gb:zm53h09.s1 Stratagene fibroblast (937	lo-hi-lo
	304309	AA112147		gb:zm64c06.s1 Stratagene fibroblast (937	lo-hi-lo
	305503	AA759177	Hs.298148	ESTs, Weakly similar to KIAA0565 protei	lo-hi-lo
	308615	AK000142	Hs.101774	hypothetical protein FLJ23045	lo-hi-lo
	309390	AW080685		gb:xc33i09.x1 NCI_CGAP_Co18 Homo sapiens	lo-hi-lo
45	104937	Al239923	Hs.30098	ESTs	io-hi-lo
	310014	D60745	Hs.25925	Homo sapiens clone 23850 mRNA sequence	lo-hi-lo
	318814	W07361	Hs.22545	Homo sepiens cDNA FLJ12935 fis, clone NT	lo-hi-lo
	321898	C04863	Hs.47191	ESTe	lo-hi-io
	331661	W52448	Hs.56147	ESTS	lo-hi-lo
50	332120	AA609684	Hs.112748	Homo sapiens cDNA; FLJ21543 fls, clone C	lo-hi-lo
00	332258	AW975028	Hs.102754	ESTs	lo-hi-lo
	107252	D60745	Hs.25925	Homo sapiens clone 23850 mRNA sequence	lo-hi-lo
	112068	A1264847	Hs.22545	Homo sapiens cDNA FLJ12935 fis, clone NT	lo-hi-lo
	117929	N51075	Hs.47191	ESTs	lo-hi-lo
55	119637	W52448	Hs.56147	ESTS	lo-hi-lo
55	123712	AA609684	Hs.112748	Homo sapiens cDNA: FLJ21543 fis, clone C	lo-hi-lo
	124560	AW975028	Hs.102754	ESTs	lo-hi-lo
	105039	AA907305	Hs.36475	ESTs	lo-hi-lo
	105039	AA907305 AA807881	Hs.25329	ESTS	10-hi-lo
60	106689	AW296584	Hs.293782	ESTS ESTS	lo-hi-lo
00	1066849	ANV296664 AL137281	Hs.293/82 Hs.17110	Homo saplens mRNA; cDNA DKFZp434C2016 (f	lo-ni-lo
		AL13/201		nomo sapiena micros, como ostrapisos capito (i	
	107071 108218	AW385224 W57550	Hs.35198 Hs.301526	eclonucleotide pyrophosphalase/phosphodi	lo-hi-lo lo-hi-lo
				hypothetical protein FLJ13181	10-11-10
65	110930	BE242691	Hs.14947	ESTs, Weekly similar to ALU1_HUMAN ALU S	lo-hi-lo
05	112098	R44714	Hs.106795	Homo saplens cDNA FLJ13136 fis, cone NT	lo-hi-lo
	112170	BE246743	Hs.288529	hypothetical protein FLJ22635	lo-hi-lo
	112902	AL035633	"Hs.129190	Human DNA sequence from clone RP5-1046G1	lo-hi-lo
	114877	AW024162	Hs.205125	ESTs	lo-hi-to
70	116312	BE379794	Hs.65403	hypothetical protein	lo-hi-lo
70	116739	H01463	Hs.93534	ESTs	lo-hi-lo
	119267	AA064970	Hs.118145	ESTs	lo-hi-lo
	120570	AA280679	Hs.271445	ESTs, Weakly similar to ALU1_HUMAN ALU	lo-hi-lo
	121176	AL121523	Hs.97774	ESTs	lo-hi-lo
75	123360	AA532718	Hs.178604	ESTs	lo-hi-lo
75	123974	NM_015678	Hs.3821	neurobeachin	lo-hi-lo
	124777	R41933		gb:yg04f09.s1 Soares infant brain 1NIB H	lo-hi-lo
	128046	AA873285		glx oh68h05.s1 NCI_CGAP_Kid5 Homo sapiens	lo-hi-lo
	128666	AA808466	Hs.103395	hypothetical protein FLJ14146	lo-hi-lo
00	130639	Al557212	"Hs.17132	ESTs	lo-hi-lo
80	130693	R68537	Hs.17962	ESTs	lo-hi-lo
	131756	AA443966	Hs.31595	ESTs	lo-hi-lo
	131985	AA503020	Hs.36563	hypothetical protein FLJ22418	lo-hi-lo
				104	

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	132932	AW118826	Hs.6093	Homo sapiens cDNA: FLJ22783 fis, clone K	lo-hi-i
	134696	BE326276	"Hs.8861	ESTs	lo-hi-i
	300967	AA565209	Hs.269439	ESTs	lo-hi-l
	301182	AW291411	Hs.192531	ESTs, Weakly similar to S00754 zinc fing	lo-hi-l
5	307102	Al699372	Hs.193247	Homo sepiens mRNA; cDNA DKFZp434A171 (fr	lothi-l
-	303132	Al929819	Hs.4055	chromosome 21 open reading frame 50	lothit
	303506	AA340605	Hs.105887	ESTs, Weakly similar to Homolog of rat Z	lo-hi-l
	303654	BE246743	Hs.288529	hypothetical protein FLJ22635	lo-hi-l
10	310026	AA278233	Hs.100691	ESTs	lo-hi-l
10	310056	AJ253072	Hs.145383	ESTs	lo-hi-l
	310353	AJ261700	Hs.145544	ESTs	lo-hi-i
	310371	AJ262584	Hs.145575	ESTs	lo-hi-l
	310430	AJ670843	Hs,200257	ESTs	lo-hi-l
	310438	AW022192	Hs,200197	ESTs	lo-hi-l
15	310455	AJ277603	Hs.145990	ESTs	lo-hi-
	310787	AW262580	Hs.147674	KIAA1621 protein	lo-hj-l
	311067	AJ587332	Hs,209115	ESTs	lo-hi-l
	311422	F00677	Hs,101316	ESTs	lo-hì-l
	311465	AI758660	Hs.206132	ESTs	lo-hi-l
20	312073	AA682393	"Hs.119237	ESTs	lo-hi-l
	312105	T81819	Hs.302251	ESTs	lo-hi-k
	312108	T82331	"Hs.127453	ESTs	ko-hi-k
	312292	AW450103	Hs.151124	ESTS	lo-hi-k
	312313	AW293341	Hs.122505	ESTs. Weakly similar to I38022 hypotheti	lo-ni-s
25					
23	312600	AW970985	Hs.290853	ESTs	lo-hi-k
	312800	Al248774	Hs.126707	hypothetical protein FLJ11457	lo-hi-li
	312821	AA699325	Hs,269880	ESTs	lo-hi-k
	313097	Al676164	Hs.201339	ESTs	lo-hi-k
20	313166	Al801098	Hs.151500	ESTs	lo-hi-k
30	313179	AA927670	Hs.131704	ESTs	lo-hi-li
	313280	AW960454	Hs.222830	ESTs	lo-hi-k
	313689	Al908810	Hs.193288	ESTs	lo-hi-k
	314146	Al827237	Hs.282884	ESTs .	ko-hi-k
	314305	AI280112	Hs.125232	Homo sepiens cDNA FLJ13266 fis, clone OV	lo-hi-k
35	314456	Al867931	Hs.164595	ESTs	fo-hi-k
	314465	AA602917	Hs.156974	ESTs	lo-hi-k
	314881	AI095087	Hs.152299	ESTs, Moderately similar to ALU5_HUMAN A	lo-hi-h
	314918	AA548906	Hs.122244	ESTs	lo-hi-k
	315043	AA806538	Hs.130732	KJAA1575 protein	lo-hi-k
40	315074	AA828284	Hs.136729	Homo sepiens cDNA: FLJ21348 fis, clone C	lo-hi-k
70	315214	AJ915927	Hs.34771	ESTs	lo-hi-k
	315344	AW292176		FSTs	lo-hi-k
	315353	A/4292176 Al373949	Hs.245834		lo-hi-k
	315439		Hs.279610	hypothetical protein FLJ10493	lo-ni-ii
45	315439	T78413	Hs.293698	ESTs	lo-hi-k
43	315528	R37257	Hs.184780	EST8	lo-hi-li
	315720	AA292998	Hs.163900	ESTs	lo-hi-k
	315772	AW515373	Hs.271249	Homo sepiens cDNA FLJ13580 fis, clone PL	lo-hi-k
	315841	AW136397	Hs.247572	ESTs	lo-hi-k
20	316042	A1469960	Hs.170698	ESTs	o-hi-k
50	318244	AJ840781	Hs.224988	ESTs	lo-hi-k
	316345	A\V139408	Hs.152940	ESTs	lo-hi-k
	316625	BE540090	Hs.122156	ESTs	lo-hi-k
	316738	AA889055	Hs.123488	ESTs	lo-hi-k
	316868	AI660898	Hs.195602	ESTs	lo-hi-k
55	316905	AW138241	Hs.210846	ESTs	lo-hi-k
	317224	X73608	"Hs.93029	sparo/osteonectin, owov and kazal-like d	lo-hi-k
	317275	AI809444	Hs,202108	ESTs	lo-hi-k
	317404	AI806867	Hs.126594	ESTs	lo-hi-k
	317488	AW071851	Hs.130628	ESTS	lo-hi-k
60	317916	A1565071	Hs.159983	ESTs	ko-hi-k
	317939	A1986208	Hs.244760	ESTS	lo-hi-k
	318486	T23514		gb:seq3329 1-NIB Homo sapiens cDNA clone	lo-hi-k
	319897	N46574	Hs.43838	ESTs	lo-hi-k
				ESIS FOR-	
65	320654 320697	AI160015 N62937	Hs.118112	ESTs ESTs	lo-hi-k lo-hi-k
05			Hs.269109	ESIS	
	320787	AW088363	Hs.246240	ESTs	lo-hi-k
	321023	AW294316	Hs.125608	ESTs	lo-hi-k
	321899	AW972832	Hs.29468	ESTs	lo-hi-k
70	322939	AA101697	Hs.211270	ESTs	lo-hi-k
70	323045	AA148950	Hs.188836	ESTs	lo-hi-k
	323091	AJ902456	Hs.210761	ESTs	lo-hi-k
	323262	AL133990	Hs.190642	ESTs	lo-hi-k
	323410	AW118683	Hs.154150	ESTs	lo-hi-k
	323645	AW445014	Hs.197746	ESTs	io-hi-k
75	324598	AW972227	Hs.163986	Homo sapiens cDNA: FLJ22765 fis, clone K	lo-hi-k
	324666	T78413	Hs.293696	ESTs	lo-hi-k
	324674	AA541323	Hs.115831	ESTs	lo-hi-k
	324713	AI093930	Hs.313466	ESTs	lo-hi-k
	324790	AI334367	Hs.159337	ESTs	lo-hi-k
80	324804	AI692552		gbrwd73f12.x1 NCI_CGAP_Lu24 Homo sapiens	lo-hi-k
	330728	AI905520	Hs.29672	ESTs	lo-hi-k
	330720	H04588	Hs.30469	ESTS	lo-hi-k
	330/00		115.30103	FOIR	10411-10
				105	

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	330776	AW953805	Hs.21887	ESTs	lo-hi-lo
	330824	AB037732	Hs.61441	KIAA 1311 protein	lo-hi-lo
	331028 331046	A1539652 NGG563	Hs. 28338 Hs. 191358	KIAA1546 protein ESTs	lo-hi-lo
5	331050	BE007967	Hs.155795	ESTs	lo-hi-lo
	331053	Al949841	Hs. 183146	ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
	331180 331313	R44692 AA761094	Hs.6640 *Hs.80618	Human DNA sequence from PAC 75N13 on chr hypothetical protein	lo-hi-lo lo-hi-lo
	331337	N74392	Hs.50495	nypomencai protein ESTs	lo-hi-lo
10	331393	AW976438	*Hs.17428	RBP1-like prolein	lo-hi-lo
	331432	AA262451	Hs.38485	ESTs	lo-hi-lo
	331517 331686	AA765603 AW474960	Hs.180877 Hs.182258	H3 histone, family 3B (H3.3B) ESTs	lo-hi-lo lo-hi-lo
	331000	Al579909	Hs 105104	ESTS ESTS	lodido
15	332043	AA371307	Hs.125056	ESTs	lo-hi-lo
	332265	AW770320	Hs.222413	ESTs	lo-hi-lo
	332314	R41396	Hs.101774	hypothetical protein FLJ23045	lo-hi-lo lo-hi-lo
	131517	ABC37789 AA604799	Hs.263395 Hs.136528	sema domain, transmembrane domain (TM), ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
20	315498	AA628539	Hs.116252	ESTs, Moderately similar to ALU1_HUMAN A	lo-hi-lo
	321489	AM59177	Hs.172759	ESTs, Moderately similar to ALU7_HUMAN A	lo-hi-lo
	108099 105726	NM_012068 NM_012068	Hs.9754 Hs.9754	activating transcription factor 5 activating transcription factor 5	lo-hi-lo lo-hi-lo
	319926	AI820719	Hs.154662	DnaJ (Hsp40) homolog, subfamily A, membe	lo-hi-lo
25	314915	A1673735	Hs.187748	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-hi-lo
	315198	AI741506	Hs.186753	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-hi-lo
	324302 331341	AW972771 BE541042	Hs.292471 "Hs.23240	ESTs, Weakly similar to ALU1_HUMAN ALU S Homo saplens cDNA FLJ13496 fis, clone PL	lo-hi-lo lo-hi-lo
	113783	AL359588	Hs.7041	hypothetical protein DKFZp762B226	lo-hi-lo
30	313552	Al889208	Hs.17283	hypothetical protein FLJ10890	lo-hi-lo
	103989	AA315993	Hs.105484	Homo saplens regenerating gene type IV m	io-hi-lo
	331492	AK001114	Hs.53913	hypothetical protein FLJ 10252	lo-hi-lo lo-hi-lo
	110837 330814	H03109 AI955040	Hs.108920 Hs.265398	HT018 protein ESTs. Weakly similar to transformation-r	lo-hi-lo
35	312226	AA315703	Hs.199993	ESTs	lo-hi-lo
	102034	AI903474	Hs.230	fibromodulin	lo-hi-lo
	134671 131063	BE263255 Y09763	Hs.302749 Hs.22785	FK506-binding prolein 9 (63 kD) gamma-aminobutyric acid (GABA) A recepto	lo-hi-lo lo-hi-lo
	309575	AW168098	Hs.169478	glyceraideltyde-3-phosphale deltydrogenase	lo-III-lo
40	134332	D86962	Hs.81875	growth factor receptor-bound protein 10	lo-H-lo
	132904	NM_005518	Hs.59689	3-hydroxy-3-methy/glotaryt-Coenzyme A sy	lo-H-lo
	302910 133731	N77976 N71725	Hs.251577 "Hs.272572	hemoglobin, aipha 1 hemoglobin, aipha 2	lo-hi-lo lo-hi-lo
	303297	AF070623	Hs.13423	Homo saplens clone 24468 mRNA sequence	lo-hi-lo
45	108732	AA258888	Hs.107476	ATP synthase, H+ transporting, mitochond	lo-hi-lo
	108731	AA258888	Hs.107476	ATP synthase, H+ transporting, milochond	io-hi-to
	302123 131614	AB013452 AB002438	Hs.144931 Hs.29596	ATPase, aminophospholipid transporter (A Homo sapiens mRNA from chromosome 5q21-2	io-hi-io
	104933	N94126	Hs.12969	hypothetical protein	lo-hi-lo
50	302235	AL049987	Hs.188381	Homo saplens mRNA; cDNA DKFZp564F112 (fr	lo-hi-lo
	320574	ALC49443	Hs.161283	Home saplens mRNA; cDNA DKFZp586N2020 (f	lo-hi-lo
	324678 331022	At990739 HG3109	Hs.77868 Hs.106920	ORF HT018 protein	lo-hi-lo lo-hi-lo
	332430	H25350	Hs.21145	hypothetical protein FLJ22489	lo-hi-lo
55	330601	U90916	Hs.82845	Homo saplens cDNA: FLJ21930 fis, clone H	lo-hi-lo
	101988	AF221521	Hs.8068	hematopoletic PBX-interacting protein	lo-hi-lo
	102859 101363	AL036058 M11321	*Hs.76807	major histocompatibility complex, class	lo-hi-lo lo-hi-lo
	133968	AA355986	Hs.232068	transcription factor 8 (represses interf	lo-hi-lo
60	332530	M31669	Hs.1735	inhibin, beta B (activin AB beta polypep	lo-hl-lo
	317777	NM_014785	Hs.47313	KIAA0258 gene product	lo-hi-lo
	100452 112988	D87742 NM_014867	Hs.241552 Hs.5333	KIAA0268 protein KIAA0711 gene product	lo-hi-lo lo-hi-lo
	320848	AB020691	Hs.198232	KIAA0884 protein	lo-ini-lo
65	105162	AL133033	*Hs.4084	KIAA1025 protein	lo-hi-lo
	133905	AB028974	Hs.137476	KIAA1051 protein	lo-hi-lo
	331406 321441	BE176893 AF107493	Hs.23440 Hs.118498	KIAA1105 prolein Homo saplens LUCA-15 protein mRNA, spilc	lo-hi-lo lo-hi-lo
	131913	AW207440	Hs.185973	degenerative spermatocyte (homolog Droso	lo-hi-lo
70	135424	U67611		transaldolase 1	lo-hi-lo
	128506	L40904	Hs.100724	peroxisome proliferalive activated recep	lo-hi-lo
	330506 311251	Al130740 Al655662	Hs.6241 Hs.197698	phosphoinosifide-3-kinase, regulatory su ESTs	lo-hi-lo
	311251	Al666662 Al821895	Hs.197698 Hs.193481	ESTS	lo-in-io
75	108096	AW379378	Hs.170121	protein tyrosine phosphatase, receptor t	lo-hi-lo
	133740	AW162919	'Hs.170160	RAB2, member RAS oncogene family-like	lo-hi-lo
	119521 119546	W38038 W38169			lo-hi-lo lo-hi-lo
	119546	W38169 W38197		•	lo-m-io lo-hi-lo
80	133797	AL133921	Hs.76272	retinoblastoma-binding protein 2	lo-hi-lo
_	305096	AA642964	Hs.163593	ribosomal protein L18a	lo-hi-lo
	120256	AA169801	Hs.98710	hypothetical protein	lo-hi-lo

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	322919 300566	AA178955 R34926	Hs.271439 Hs.326392	ESTs	lo-hi-lo lo-hi-lo
	330694	AJ741617	Hs.326392 Hs.108447	son of seveniess (Drosophila) homolog 1 spinocerebellar ataxia 7 (olivopontocere	lo-m-io
	302416	AL120259	Hs.76691	stantin	lo-hi-lo
5	319289	AA037534	Hs.79059	transforming growth factor, beta recepto	lo-hi-lo
	134656	AI750878	Hs.87409 Hs.150207	Ihrombospondin 1	lo-hi-lo lo-hi-lo
	124357	U08641 N22401	HS.150207	UDP glycosyltransferase 2 family, polype gb;yw37g07.s1 Morton Fetal Cochlea Homo	lo-ni-lo
	108293	AA069155		ob:zm10f11.s1 Stratagene pancress (93720	lo-hi-lo
10	108657	BE567753	Hs. 132955	BCL2/adenovirus E1B 19kD-interacting pro	lo-hl-lo
	108658 331278	AA641695 AA071383		gb:nr62h10.s1 NCI_CGAP_Lym3 Homo sepiens	lo-hi-lo lo-hi-lo
	108340	AA069820	Hs,180909	gb:zm61d05.r1 Stratagene fibroblasi (937 peroxitedoxin 1	lo-tri-lo
	108679	AA115963	Hs.323423	ESTs, Moderately similar to B Chain B.	lo-hi-lo
15	108406	AA075424	Hs.325505	ESTs, Moderately similar to HBA_HUMAN HE	lo-hi-lo
	114598	AA075601		gbrzm68c05.r1 Stratagene ovarian cancer	lo-hi-lo
	108462 108466	AA079347 AA079409		gb:zm96c06.s1 Strategene colon HT29 (937 gb:zm96h02.s1 Strategene colon HT29 (937	lo-hi-lo lo-hi-lo
	108489	AA082977		gb:zn07h10.r1 Stratagene hNT neuron (937	lo-hi-lo
20	330859	AA082977		gb:zn07h10.r1 Stratagene hNT neuron (937	lo-hi-lo
	108505	AA083376		gb:zn09g06.s1 Stralagene hNT neuron (937	lo-hi-lo
	331283 100641	AA467736 AW068302	Hs.275437 'Hs.182183	ESTs Homo sapiens mRNA for caldesmon, 3" UTR	lo-hi-lo lo-hi-lo-hi
	100642	AW068302 AW068302	*Hs.182183	Homo sapiens mRNA for caldesmon, 3 UTR	lo-hi-lo-hi
25	325889	ANOUGUE	110.102100	CH.16_hs qll5867087	lo-hi-lo-hi
	338038			CH22_EM:AC005500.GENSCAN.149-9	io-hi-lo-hi
	338316			CH22_EM:AC005500.GENSCAN.304-2	lo-hi-lo-hi
	100999 331131	H38765 R54797	Hs.80706	disphorase (NADH/NADPH) (cytochrome b-5 gb:yg67b07.s1 Soares infant brain 1NIB H	lo-hi-io-hi lo-hi-io-hi
30	310955	Al476732	Hs.263912	ESTs	lo-hi-lo-hi
	311137	AW207582	Hs.196042	ESTs	lo-hi-lo-hi
	311598	AW023595	Hs.232048	ESTs	lo-hi-io-hi
	313070 110844	Al422023 Al740792	Hs.161338 Hs.167531	ESTs methylorolongyl-Coenzyme A carboxylase 2	lo-hi-lo-hi lo-hi-lo-hi
35	120328	AA923278	Hs.290905	ESTs, Weakly similar to protease [H.sapi	lo-hi-lo-hi
	105914	AW245680	Hs.9701	growth arrest and DNA-damage-inducible.	lo-hi-lo-hi
	129389	NM_012445	'Hs.288126	spondin 2, extracellular metrix protein	lo-hi-lo-hi
	102759 100168	NM_005100	Hs.788	A kinase (PRKA) anchor protein (gravin)	lo-lo-hi Io-lo-hi
40	102348	H73444 U37519	Hs.394 Hs.87539	sdrenomedullin sldehyde dehydrogensse 8	10-10-N1 10-10-hi
10	134158	U15174	Hs.79428	BCL2/adenovirus E1B 19kD-interacting pro	lo-lo-hi
	133906	AU076820	Hs.325474	caldesmon 1	lo-lo-hi
	101883	AU076743	Hs.75613	CD36 antigen (collegen type I receptor, CH.05_hs gij5867968	lo-lo-hi lo-lo-hi
45	134133	AA262294	Hs.180383	dual specificity phosphalase 6	lo-lo-hi
10	103000	NM 001975	"Hs.146580	enclase 2, (garwina, neuronal)	lo-lo-hi
	109251	AA194776	Hs.85935	EST	lo-lo-hi
	315566 324697	AB037810	Hs.18760	KIAA1389 protein	lo-lo-hi
50	306011	AK000742 AA896966	Hs.126774	L2DTL protein ob:a106a08.s1 Barslead spleen HPLRB2 Hom	lo-lo-hi lo-lo-hi
50	307111	Al174528		glxan45g10.s1 Gessler Wilms lumor Homo s	lo-lo-hi
	106639	AV655272	Hs.20252	novel Ras family protein	lo-lo-hi
	106753	Al656166 AW956103	Hs.7331	hypothetical protein FLJ22316	lo-lo-hi lo-lo-hi
55	107974	R49031	Hs.61712 Hs.22627	pyruvele dehydrogensse kinase, isoenzyme ESTs	io-io-ni io-io-hi
55	113816	H46008	Hs.31518	ESTS	lo-lo-hi
	118024	AA088767	'Hs.83883	transmembrane, prostate androgen Induced	lo-lo-hi
	116158	AA381807	Hs.61782	hypcoda-includible protein 2	lo-lo-hi
60	119071 120132	R31180 W57554	Hs.125019	gbcyh62b02.s1 Soares placenta Nb2HP Homo ESTs	lo-lo-hi lo-lo-hi
00	120655	AA305599	Hs. 238205	hypothetical protein PRC2013	lo-lo-hi
	122411	AW172356	Hs.99083	ESTs	lo-lo-hi
	320779 321024	AA815354	Hs.169696	ESTs	lo-lo-hi lo-lo-hi
65	321024	AW246216 AW081530	Hs.32058 Hs.137088	Homo saplens C1orf19 mRNA, partial cds ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-ni lo-lo-hi
05	323620	AA306997	Hs.268362	ESTs, Weekly similar to hypothetical pro	lo-lo-hi
	314946	Al097229	Hs.217484	ESTs	lo-lo-hi
	320683	AA334511	Hs.26638	ESTs, Weakly similar to unnamed protein	lo-lo-hi
70	128959 128896	Al580127 T53925	Hs.107381 Hs.107	hypothetical protein FLJ11200 fibrinogen-like 1	lo-io-hi lo-io-hi
,,	133592	AV652086	Hs.75113	general transcription factor IIIA	lo-lo-hi
	103245	BE566343	"Hs.28988	olutaredoxin (thiottransferase)	lo-lo-hi
	314785	Al538226	Hs.32976	guantne nucleotide binding protein 4	lo-lo-hi
75	103677	Z83806	"Hs.23796	gb:H.sapiens mRNA for acconomal dynain he	lo-lo-hi lo-lo-hi
13	131170 131164	NM_014253 AW013807	Hs.182265	odz (odd Oziten-m, Drosophila) homolog 1 kerstin 19	io-io-ni lo-lo-hi
	100409	D86957	Hs.80712	KIAA0202 protein	lo-lo-hi
	133167	AW162840	Hs.6641	kinesin family member 5C	lo-lo-hi
80	319080 330706	AW967646 AF097994	Hs.23023 Hs.301528	ESTs L-kynurenine/alpha-aminoadipate aminotra	lo-lo-hi lo-lo-hi
00	330706 104052	AF097994 NM_002407	Hs.97644	L-kynurenine/alpha-aminoadipate aminotra mammaglobin 2	lo-lo-hi
	100547	M57417		gb:Homo sapiens mucin (mucin) mRNA, part	lo-lo-hi
				107	

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	103145	X66276	Hs,169849	mycsin-binding protein C, slow-type	lo-lo-iti
	301015	AV655272	Hs.20252	novel Ras family protein	lo-lo-hi
	311013	AA224760	"Hs,153	ribosomal protein L7	lo-io-hi
	132050	Al267615	Hs.38022	ESTs	lo-lo-hi
5	132349	AW975654	"Hs 181286	serine protease inhibitor, Kazal type 1	lo-lo-hi
	130889	AW972512	Hs.20985	sin3-associated polypeptide, 30kD	lo-lo-hi
	130791	AF030403	Hs.199263	Ste-20 related kinase	lo-lo-hi
	130385	AW067800	Hs.155223	stanniocalcin 2	lo-lo-hi
	127229	AA316181	Hs.61635	six transmembrane epithelial antigen of	lo-lo-hi
10	133820	\$69681	*Hs.177582	surfactant, pulmonary-associated protein	lo-lo-hi
	129523	M13231	Hs.274509	T cell receptor gamma constant 2	lo-lo-hi
	321415	BE621807	Hs.3337	transmembrane 4 seperfamily member 1	lo-lo-hi
	131859	AW960564	"Hs.3337	transmembrane 4 superfamily member 1	lo-lo-hi
	133444	M63978	Hs.73793	vascular endothelial growth factor	lo-lo-hi
15	332567	AW939251	"Hs.25647	v-fos FBJ murine osleosarcoma viral onco	lo-lo-hi
	131328	AW939251	*Hs.25647	v-fos FBJ murine osfeosarcoma viral onco	lo-lo-liù
	315901	AJ521558	Hs.7331	hypothetical protein FLJ22316	lo-lo-hi
	104394	AA129551	Hs.172129	Homo sagiens cDNA: FLJ21409 fis, clone C	lo lo hi
	103739	AA115173		giczn30d02.s1 Stratagene neuroegithelium	lo-lo-hi
20	103797	AA080912		gb:zn04d03.r1 Stratagene hNT neuron (937	lo-lo-hi
	103804	AA129196		gb:zn29d06.r1 Stratagene neuroepithelium	lo-lo-hi

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TABLE 1B

Pkey: Unique Eos probeset identifier number CAT number: Gene cluster number Accession: Genbenk accession numbers

5	Accession:	Genbank access	ion numbers
10	Pkey 108462 108489	CAT Number 116651_1 118662_1	Accessions AUTISMT AUTISEDS AUTISMS AUTISMS AURISMT AUTISEDS AUTISMS AUTISMS
10	101216	17379_1	AUZBEING ANJATIFUT LESTELL ZITTI I AMERITAN ENGER I WURSEN I ANJATIFUT BESSIES IZ I AMERIKAN DOS 122 ATTS 13.5 AMERICA I AMERI
15	131328	8509_1	AND SECTION THAT DESCRIPTION AND SECTION ASSOCIATION AND SECTION ASSOCIATION AND SECTION ASSOCIATION AND SECTION ASSOCIATION A
20			AMTSBESS AMTERISEN TRESSES FIRSKEYS ABOOZETS AMOODSSES AMTERISE AMTHER BEZZESS AMTERISES AMTERIS
25			A/MERICA BITATE A MAZOTA BASTORI ALBISTIA AWAZOTA SA TITA AWAZONO AKBAZON BASTOZA ABATIZA RAZZIFE ABAZTIZA SA MAZOTA BASTORI AWAZONA BASTORI AWAZONA BASTORI AWAZONA BASTORI AWAZONA BASTORI AWAZONA AWAZONA BASTORI AWAZONA AWAZONA BASTORI AWAZONA AWAZONA BASTORI AWAZONA A
30			AISTTRIA MASTERIA AIZMARZA KARAGIKA MASZETIR MARRISKE AIRIKKEN DEGIOTO MARKESIA MAKARISKA TIRIKA TIRIKA MATRISKA TIRIKA TIRIKA MARKESIA BERDINGA TIRIKA MARKESIA BERDINGA TIRIKA MARKESIA TIRIKA TIRIKA MARKESIA TIRIKA MATRISKA TIRIKA TIRIKA MARKESIA TIRIKA MATRISKA TIRIKA TIRIKA TIRIKA MATRISKA TIRIKA TIRIK
35			AZZYASIA DETIZZA DESIGE DESIGE DEZIZA DESIGNI AMERISES SALVERAN DESTIZ RETA'NO ECHI SES DEZIZA ANTISESA DESIGNI AMERISES DESI
40	124148	31218_1	T18515 AVXIOZETÉ ALAGUSE (1832) AUXINITS VOIS 12 VOI 512 AVSTAUT AVXIS LA ARSTAUT DE 174851 ASSRUZ AZE REST RESSO ALAGUEZ MESSE AVITSUTA BEXXIONA (ECUANA) AVITSURA (1814) (1812) AVXIO (1814) AVXIO (1814) AVXIO (1814) AVXIO (1814) AVXIO (1814) AXIO (1814) AXI
45			X15556, DAMES A-BERSSEZ HASTYDD A MASBEST S-ABTISKS INKEZTI A-MODELA XMERBES BEVLE SA BERSSEZ A-MEDISS B-ABSZYSS INVEST ANDERSSE ANDERSSEZ A-MEDISSE ANDER THE BEVER SERVES MEDIZSE FESTER A SERVES BERSSEZ XMEST ANTASSES ANDERSSEZ ANSSEZIA INKEZTI SET ZOTRE A-MAZIZSA INVISITUS ANASSESS ANDERSSE VIZISSEZ XMEST ANDERSSEZ ANASIZSA SERVES ANDERSSEZ XMEST ANDERSSEZ ANDERSSEZ XMEST ANDER
50			ANDCOST PAGESZES PAGES AND FACE SESSES ESTENDING HER ESTENDING HERCOTOR AND FACE AND AND FACE SESSES AND FACE
55			Wed41 A (2005) A (2015) A (201
60			AASTYSS A689112 AIRTZOSA AASSARSIA ARKSEKS AIRSEKS AIRSEKS ARKST AKTI AKTI AKTI AKTI AKTI AKTI AKTI AKT
65			HEMBER AND PRISES AND
70			AASISSH HISSHE HISBET ARBUSS AH IZBED AASISHS ANTERBE FT-MET FS-MASS AASISH IZBET ABS
75	124153	25750_1	1808352, 3415455 HELD DIEGO STOREY REMEI BER JAMEN LERGE TESSES, BAJZELES PLANESTES PLANESTES ALLES BAZILESS
80			AVM-68/2 AVMC/2000 ASSTRAT AACSTTS AVM2020 MT346S AAATTSS AVM102016 AASBERS TWO HOT DE EPTASD 17/23/11 T87/221 AA106001 101000 AMBRECOM AOSBERS AASTTS AAAATTSS AAATTSS AVM102016 AASBERS TWO HAVETS TO STA AATTST AAATTST AAA

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W42964 AA384428 AW994316 H95163 H95158 R33688 W46557 AW748451 AA029916 AA463826 AA314287 R23084 AA368891 H02926 AA310456 H03632 C02397 R63745 H94539 R32226 R2M648 H44502 AA039671 AA345336 W42846 R46024 R79724 R63143 AA379513 R21780 R80704 T70422 H21580 H46388 R62779 AA579734 N64111 AA344527 AI865473 R66666 Z20058 T52284 H95103 R36513 R21874 R31363 AA220939 BE439695 A189683 AA164901 A/539383 AA768249 AA442361 W02867 AA303315 AW952009 AA314544 A/076799 5 AA216780 T70338 AA039672 AW629489 AL044620 AA533203 AA043082 Al668619 AW298204 AW195268 AL391606 AA437282 AW304801 AW085720 WV2586 AA853279 T82339 AI366879 BE464557 AI038992 AI190018 BE146083 AI860399 AI039572 AI129687 AW468134 AI436074 A 3933509 AI682339 AW663467 AW129657 AA660298 AA460262 H91217 NS7879 R66069 N95684 AA040855 AA2Z1116 N94486 H04229 H97677 A161080 A0X4367 A0025767 A075485 AA688150 A355979 R79463 AA029917 R89637 A1810134 AA468820 A3377990 AI743170 AA854637 AA628549 AA664223 AI362196 AA489363 AI361404 AI363155 AA300504 AI678269 AA633851 H61743 AI161012 10 AW339721 W42847 W46558 AA143120 Al042475 AA479365 AA219592 AW468142 H67690 A186516 AA531387 AA835378 H03030 T68119 H95133 AL040491 Al289149 R63701 R32177 R32865 Al811374 Al613274 AA775300 AW192882 R37509 W42965 R47918 Al949525 Al129450 H49376 AI435907 AB32271 AA479271 R21949 H03633 AI888539 C75673 AI261394 AA614476 AW463907 AI261429 W03148 AW026141 AW236371 R79725 AA34666 C06197 127764 H58538 AT74196 AA485299 AA719227 AI688762 N70790 AI825028 R21734 AA977432 H77905 AI625648 AAS18668 AI220069 AI362568 AA668729 AA195395 T63334 AIS32783 N32271 R26048 H90697 R24539 AI970287 T55374 15 N93019 T11162 AA377400 AW862126 AA602293 F35923 AH24237 AR26517 H27442 AA039729 AA382630 AI567304 AA045112 T57779 AJ474576 AJ352569 R63095 H44456 X85116 AJ521609 AA164352 BE146079 H60082 AJ334776 AA700506 AA782742 R67386 R22978 R33584 R67011 R80705 Al245311 H81590 Al360786 Al219244 R39564 H66850 Al184385 AA697691 H68013 AA092081 Al445480 AW005734 AW068302 A/754558 A/750727 A/752631 AA302174 AA302174 NW66398 AW66989 A/75195 AA769520 A/858829 A/924875 AW88838 AA664591 A/68960 AW66039 A/924908 AW466398 A/924800 A6961651 A/924601 BED04703 AA34442 A/M268952 A/194330 100641 28620_1 2.0 ALD46953 A-882966 AW391995 W30846 AW662928 W25291 A-0A/2863 R99045 H37/60 W03910 H94697 T89891 ALD48165 T29632 N31556 N38484 Al798679 A-089355 W23932 A-8873799 Al743646 A-363587 AI814748 AW338990 N73740 N3366 ALD47816 R24137 R6343 AA524984 AA234043 AA195131 N99903 AA453669 AI240302 AA370271 AI950026 AWTT1049 AA121476 AA569557 AI752632 AI355 A|471993 A|159941 N94555 A|753138 N21537 H97881 N25769 AW068044 AA808425 R63380 AA384736 AA384738 AA852352 A|073645 ASSZYBIO AACSZGG AADIA414 ATISZAGO AATGOOD RIDZIS AARSZTSIO AATGOOD RIDZIS AARSZTSIO AATGOOD RIDZIS AARSZTSIO AATGOOD RIDZIS AARSZTSIO AATGOOD AATGOOD RIDZIS AARSZTSIO AATGOOD AAGSTOOD AATGOOD AAGSTOOD AATGOOD AATG 2.5 AA318496 AA318213 AA318436 AA318424 AA318217 AA318523 AA318487 AA318774 AA593185 AA994985 TS9942 A318217 AA3185486 AA31847 AA318774 AA593185 AA994985 TS9942 A318523 AA318487 AA318774 AA593185 AA79777 TS8390 F97712 AA121145 H08973 AA345217 BE000667 AW068210 AW605407 R05674 H16712 N85428 H42354 H85516 BE147991 T28113 R32662 AA384678 AW339275 H8282 AW604700 D58229 C04082 W45394 AW759687 R73973 BED02409
AA042328 AA363555 AJ23812 AA344709 BE149590 R7095 W46881 W90778 N71242 AA34828 AL04676 R23797 H96450 AA062957 30 ANGEGES ANGELOS AUSSILOS AUSSILOS AUSSILOS SE REGIONAL PUESOS PARASON TO SE TO TATAL AUSSILOS AUGSILOS AUSSILOS AUSSILOS AUSSILOS AUSSILOS AUSSILOS AUGSILOS 35 AW069069 AW069454 AA342989 Al077712 Al311467 Al087361 Al801015 W46993 Al281324 AW191963 Al421675 Al300881 Al356670 AA873156 Al004219 Al189685 AA478018 AA076063 Al445222 Al753124 Al521569 Al925026 Al022368 Al475993 H20846 Al223234 Al635123 AA579170 N30442 AW117889 AA807935 AA558975 AJ00636 AA888963 AI952591 AJ935835 AI445293 H18713 AW139833 AA522122 AA972051 AJ280828 H09543 AM53725 AW069613 AI865615 AJ753921 AJ368782 AI633208 AJ446651 W46961 N22201 H82276 C16555 AA2914T7 AW440556 AW517756 A4669921 AI926T77 AW662118 (A553399 NG7873 AW023948 C15861 C16601 AI251465 AW/079167 BED45090 AI273036 C16390 C16503 AI620823 F13661 N66864 Z2:311 C16108 C16089 C16400 AA758273 AI287781 AA884878 AW/08074 40 AW385583 AI589944 AA665817 AW192979 AW469065 AA564048 H84715 C16417 AA731072 AA661674 C16487 N29477 AW189997 AJ370492 C16471 AA652809 AA936687 AA506512 C16306 AW028413 AJ537935 AA528347 C16255 AW029046 C16202 AJ868152 AJ524662 45 AV659047 AV659632 AI750389 AA092053 AA092798 H85367 T61597 R23745 Z20418 T78485 AI751528 AW068121 AA853188 AI752459 AA853711 AW950563 R78964 R36359 R21626 R21522 100642 28820_1 AW088302 AI754558 AI750727 AI752531 AA302174 AA327522 M64110 AW859944 AW859989 AI751995 AA769620 AI858829 AI924675 AMMERICA AMBIGOR MANIOR MANIOR AMBIGORY 50 AA527980 AA525036 AA044414 AJ752460 AA703064 R01216 AA697183 AJ751996 TB1078 H95047 AA573642 D58348 N20953 AA437143 55 NS5439 AA579540 AW867056 AA770050 Al085190 Al086799 AA425421 Al572613 R24081 AA863189 AA295520 AA234044 AA371020 AVES4984 120095 AW384438 AA316516 AA316499 AA316727 AA316211 AA316478 AA316444 AA316307 AA316487 AA316446 AA316309 AA316189 AA318213 AA3161436 AA316442 AA31627 AA316524 AA316458 AA316487 AA316548 FAA31672 AA316548 AA316318 A AA476174 AA46737 TBG306 POT712 AA421146 H00973 AA346212 BEDOOMST AW068210 AW06807 ROSST H H01712 1864568 H2536 H85516 BE147991 T28113 R32662 AA384678 AW239275 H82382 AW840700 D58229 C04082 W45394 AW795667 R73973 BE002409 60 AA042828 AA363555 AJ228812 AA344709 BE149590 R70995 W46881 W90778 N71242 AA534826 AL040676 R23797 H96450 AA062957 D78947 W46980 AW959278 AA298987 AA026215 AW579499 AW365135 AW965134 AW994363 AW972886 AW059166 AA343690 AW888731 AI751527 AA937490 AA937506 AI826715 BEA65604 AI925532 AI858109 AW339097 AI858524 AI720571 BE046506 AW384981 AA043908 AA375983 AA525181 AW068366 AW070577 AW891837 NB3985 AW182753 AI422979 AI679733 BE006555 AL048166 AI081401 AI888821 AND/1985 XH523161 AVR06508B AVR04101 AMM651 OF TRASSES AW 162/503 AVA265755 AIB1480 AIRS26043 AVX06575 AIB24140 AIB01238 AA600048 AI753947 H89615 186424 AVX065755 AIB1480 AIRS26043 AVX06575 AIB14816 AVX065059 AVX0650 65 AA873156 A1004219 A183685 AA479018 AA076063 A445222 A1753124 A1521569 A1925026 A1022366 A1475993 H20846 A1223234 A1535123 AA579170 N30442 AW117889 AA807935 AA558975 AI308536 AA88963 AI952591 AI308535 AI445293 H16713 AW139833 AA622122 AA972051 A1280828 H09543 A453725 AW069613 A1866615 A753921 A368782 AK33208 A1446651 W46961 N22201 H82276 C16555 AA291477 AW440535 AW517755 AA669921 A1926777 AW662118 AA553369 N67873 AW023948 C15861 C16601 A1251465 AW079187 70 BED45090 Al273006 C16390 C16503 Al620823 F13661 N66864 Z21311 C16108 C16089 C16400 AA758273 Al287781 AA864676 AW608074 AW385383 Al589944 AA665817 AW192979 AW469065 AA564046 H84715 C16417 AA731072 AA661674 C16487 N29477 AW189997 Al376492 C16471 AA652809 AA936687 AA506512 C16306 AW028413 Al537935 AA528347 C16255 AW029046 C16202 Al868152 Al524662 T94414 AJ567041 AJ619554 AW008486 AJ075624 AA577434 AA345104 T30105 AA932002 C16585 AJ750390 AW294265 AJ619552 AA669781 AA028678 AW192002 AW263919 C16562 AA759137 AA693351 Z40779 C16577 AA695045 AW073763 R45484 AI520895 U54708 T49285 75 AI568126 AW006569 AI093317 AL119781 T61046 AI053563 H51958 AF114144 AA305739 AW950394 AW793928 AW793910 AL047737 AV559047 AV659632 AI750389 AA092053 AA092798 H85367 T61597 R23745 Z20418 T78485 AI751528 AW068121 AA853188 AI752459 AARS711 AW950863 R78964 R36359 R21626 R21522 BE250162 BE298066 NM_002439 U61961 AA421716 AA723916 N32298 H99382 AI817671 AW364509 AW364468 BE250719 AW364498 100656 10385 1 80 AA427637 J00146 AA252992 AI784131 AA694127 Al352150 AA250600 Al040148 Al090860 AA215895 AA227746 Al040147 AA401306 Al332971 Al187739 AW013865 AA010576 AA699792 Al131225 AA700469 R91775 AA778381 AA455309 R00884 T91344 AA682438

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10	124182	437383_1	AASS-961 AA927195 A274415 AA56221 AISS7471 AN/511357 AIS750-7 AA568500 AI25-413 AA913457 H48062 AI218202 H80118 W58272 AI243058 AI08307 AW470886 AA757972 AW89465 AI652036 AI652469 H68711 W88721 H78771 H48762 AI218202 H80118 W58272 AI243058 AI088307 AW470886 AA757972
	116312	12146_1	BE379794 NM, 016629 AF208860 AA156366 AB07277 H41872 BE155971 AW380559 AW026522 AW337 168 AW338644 AA181032 AW571620 A160161 AA555059 A469445 A304501 AA621819 AI218750 AA993112 AA989022 AJ913199 A1863142 AA554244 AA885980
15	100676	21764_1	AVIOCUS A ARESDEA HABBORS HABBORS AVETTERS AAA60044 AA66273 TI 1762 AA67175 AA86066 AVESSOO ALGOS ISA SAVOSGOS AVETTERS AA66044 AA66273 TI 1762 AA67175 AA67175 AVETTERS AVETT
20			C1972 UG204 ANS/3884 AWS86570 BE17425 A860/010 AW750514 A1356556 AITS0644 T47698 P81777 T462/5 T930/8 R33/50 T49421 AW303099 AURE2805 BE142894 A4125277 188780 AU7503351 H43251 A330915 R23/40 AA367947 AW698522 1/2531 9 AA935923 AM362761 H75633 R15240 A750474 T78689 R62612 T52447 U41690 U42256 AW99/490 W25621 R21374
	130760	7278_1	AW379130 BE465904 AA502909 AA558701 A1140490 AA551857 AI814897 AA964355 AA535891 AW131779 AA157947 AA128997 AA160913 AA364907 R45187 AW341841 AF048837 NM_002606 AF067223 AB017602 R19767 AI243073 R00719
25	116334	158046_1	AL038450 N66939 AA805447 AA935480 AW472717 AA176686 AA176900 AA491457 AR005269 AR377928 A/684566 N64278 AW978200 A/969917 AW937673
20	130791	30310_1	AF339.04 AF95999 NIM, 01323.3 M/MOMEZ AL65/TTR. AA251598 AI85577 A AZ2122, AISS 194.9 AA16038 AA65073 AA27339 A185073 AIBS22 28. HS182 A186577 A A26558 AA65679 AA65678 A36149 A86024 A18740 AR27662 A32767 A101518 AW6522 A185578 AV67242 SAVESZ763 A491000 A189891 AA766000 A468620. AA626461 A016857 AA61514 AA642462 AA165717 AA526390 AA26678 AA25004 AJ276578 AV685077 AA26678 HA6464 AW6520 AA52664 A37566 AA5710 A670738 AA465678 AW65857 AA615147 AA65678
30			AASISTEY ROSSTS AASISSES BEST IS HELDO AASISTEI AAH 1920 HEZDTT 186250 HEZDTT 186250 AASISTEI AAH 1920 AASISTEI AAH 1920 HEZDTT 186250 AASISTEI AAH 1920 AASISTEI AAN 1920 AASISTI AAN 1920 AAN 1920 AASISTI AAN 1920 AAN 1920 AASISTI AAN 1920 AASI
35	116357	18555_1	AMERICAN HARTI (RIGNER) ANCISSER (14419) AMERICAN HARTING ANCISSER (14419)
40	130796	49038_3	TBO2T M6455 H11738 AAMBBB99 AASTIR AMSSERT YB': 510 AWSSISSE R38527 R38090 AA216276 AA327415 AAAABSTD AWSSIGS AUS 1665 A F16558 AWSSIGS AWAY7556 R26565 AAKSSEY AAASTIR AMSSIGS AB 16050 R2655761 AB7122 R26555 AA 51555 H66555 AASSEST BASEDT BSS 113 AWSSIGS AWAY7566 R26565 AAKSSEY AAASTIR AMSSIGS AB 16050 R265576 AB7122 R3755 AASTIR AWSSIGS ABSTIR BSS 113 AB7125 AB71
45	109141	40042_1	AW135098 AA907768 A1201833 R38314 AA465584 N62420 AA904266 BE092859 A1762009 AA827837 AA465228 AA430754 AW390464 AF174600 AA176679 AA176413 AA176428
	109166	12792_1	A219991 AF153329 A4179617 AF00672 M., 005733 A4157665 AA157657 AW617662 AW633005 AW075835 A855312 A653243 AA731744 A188536 AA704870 AW690208 A671173 AA781482 BED90424 A1669341 A1203090 AW103151 A/654412 A1166283 AU014654 AW017406 A4600977 A473647 A4178945 AW074368 A4630744 A4789069 AW701368 AW074762
50	115761	18573_1	AA369337 AA393228 AW966485 BE382385 R53711 AA244040 AA340690 AA706628 W32795 AI917370 AA421612 AW341435 AW074334 AW631200 W84481 AA421374 W84326 AI358466 R52931 AID03131 AW856014 AW856057 AW856070 AW964001 AW855994 BE563579
	115784	18581_1	AW582258 AW958284 AF038451 NM_006408 AA316115 AA315629 AW358380 AA314225 AF007791 AA421527 BEJ72059 A1817063 AW194118 AW192785 A075324 AA296537 A634717 A380637 AW151674 A188294 AW190656 AW364247 A000640 AW152548 AW002338
55			AWS-1674 AM-4693 A828362 AAST7812 AM66789 AM59646 ATST6TET AW60001 AM576838 AW3884 AM5601 T EETF656 EED4201 AM57861 AWAY AWS-1674 AW5761 AW5761 AW5764 AW57
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35	123974	3842_1	NIL_015678 AL:37748 NE0380 A.335753 AW954010 AI004739 AI652524 C14642 D52944 C14716 AA775779 H15/23 C14834 H22896 RA496 AV/25661 B70360 R00679 AA510624 F00575 A450624 R04710 AA400540 AI750071 R23514 AI168314 BE326200 AI611086 AA405641 T16464 B70864 AI61023 AW61887 R06080 AA971494 R3444 AI22310 B25866 H24/234
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50			ANJ37357 EC375761 AB54606 AN12960 AN084750 BC36045 AN020868 BC343949 AA047036 A23005 A334510 BC222094 AA34008 ANJ575817 AB51299 A1765943 A1203151 AA682500 BC34646 A1681849 AA062380 AA301870 AN957983 AA729175 A1624658 AN026429 AL043046 AV966716 AA32244 AN956320 BC161834
	133050	12035_1	X7349.657255. AJ006487 NM_000528 R15273 AA312224 BER0931 AW6500PA IN15302 AA371198. R25544 AM65287 W58945 M15373 C75158 R03794 A4002221 AA609000 T27695 AW016022 AA550631 AW6500PF AA459122 AA667219 AA506463 AW7534 AA507221 EED43232 A680312 AW7467 H03980 A660311 AA419455 AA690631 W68052 A1768259 R12384 AW079484 AA222335 A1802342 H15697
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65	133063	198877_1	AIGG4133 AI7G1596 AIGB1308 AW022404 DE246846 D62530 AI472301 AW625492 AI290922 AI241788 AW118080 AI221713 AI367429 AA885741 AA807330 AW517831 AA749008 AA631276 AA838065 AA646947 H43330 AA721409 R35006 AA503266 AW511687 AI382427 AW971014
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10	131859	3672_1	AW803098 ALGORIZO AMBISAZZI DE 2800202 AW80-6227 T10085 EBER1600 EBDRIJOR AW803001 ALTITURA WINGSOS AMANGAZI TO AMBISAZZI SANDA AMBISAZZI SANDA AMBISAZZI SANDA AMBISAZZI SANDA AMBISAZZI SANDA AMBISAZI
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	131877	25130_1	JAVASS NM_001057 AG771747 AG11747 NSSL02 NDXC407 AA218572 BE206748 BE08/3881 AUG06877 AW96918 AW75045 H17813 BE081233 A4670403 AW574327 BE094229 AA104024 AW71482 AIS70337 AA737616 AIS27444 AW000286 AI742333 A34044 AI75634 AJ948838 AW7235336 AW172827 AA096289 BE046380 AI734240 W 16689 AI860329 AI7689433 A4903778 AW7469242 AA468838 A4095983
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			AD41851 N70220 A079383 A4189863 W62220 A086786 AW993698 R9681 R32011 AA828169 AV067934 A095379 R32003 A074036 R01297 A418340 AW89450 AW859699 A464310 R89956 A368816 B6218044 A086986 A872179 A4168319 F87118 A182803 A418340 F70099 A4868257 A0058517 A4128374 A4100313 F911797 F02705 A4384790 A4054935 189289 A4548517 BE621281
65			AUDBIRSS OTHEZ ABBADIS MITISIOS AWS1600 AAC2841 AMS822 ABSZETS AAT7810 BET119TS ABBBESS MISSP441 AWS9832 ABSZETS AAT7810 BET119TS ABBBESS MISSP441 AWS9832 ABSZETS AWSTERS AWS182
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30	103069	23881_3	AIBS76ST AING1S768 AM170288 AI3S4983 AING90763 AIN004962 AM079623 AA662510 AI611709 AIN117738 AA642581 AIN272971 AIN901049 AIN238343 AM286603 AI832277 AA589696 AIN0049602 AN246000 XX7361 AA654929 XCX490 B2596466 BE653963 T69724 T73068 AIN96C005 AIN994424 BE157475 AIN382565 R28460
35	103076	13655_1	NO, 00/03/ 3/98/19 EXZYTAT ANAXORON ALSH 119 ANAXOR 2425 EEST 2425 EEST 2435 EEST 2525 EEST 2525 EEST 2527 ERSH 2475 EEST 2435
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75	132543	4172_1	BERGATS AND 1982 BERSAND RE20238 AAA45692 AWY 22400 AW0397A BEFSH857 AAD17228 APA4489 NAL_00389 BE 258594, AW44579 AAA71151 BESSOTT AWY 22553 AAA74682 E 258596 AW0397A A415195 BESSC125 AA31064 AW03897T AA312729 AW75022 AW7502 AW75
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5	102469	28114_1	AFREESE INC. 001365 USPIES NOVIZETIO FAFOLOCA ANNIGEZIE ANNIGEZIE ERETZEY "11161 AMSOTSE RESELS ALOI (1864 AMDZEAU LEHRE AL ADASSE ANNIGEZIE AMSOTSE LEHRE (1861 111 HARDEN ANNIGEZIE ANNIGEZIE ERETZEY "11161 AMSOTSE RESELS ALOI (1864 AMDZEAU ASIS (1654 AN 1612) AMSORDE ANDIGEZ NOVIZED ANNIGEZIE ANNIGEZIE ANNIGEZIE ANTIGEZIE ANDIGEZIE A
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	131985	113870_1	AW973949 AA523677 AA229207 AI734061 AA614244 AA688115 AA658025 AA532387 AW973151 AA534173 AI669704 AA659396 AA652812 AA503020 AI858190 AI666571 AW615203 AW073686 AW172459 AI828762 AW150534 AI859795 AA411046 AI539195 AA404609 AI638559
40		_	AA434329 AA171844 Al684143 AA953518 AW470108 AI870700 AA706376 AI539668 Al683712 AA075579 AI682137 AA291512 AA554431 H51315 AA404225 AA075632 AA172293 H51911
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50			AADS3191 AP007133 AW02598 T77105 AW037394 AW067225 AW059920 AW359003 AW359003 AW359014 AW0598967 AW359050 FH0375 AAT13805 T8522 T8687 T81888 AY370900 AR278194 A981297 T8088 CREZIT T3 T9077 SROWLA AW75574 AW76112 EB02725 EB02757 IAW405390 AW10199 AA159021 R10051 AW359513 AW12786 AW55904
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60			ANCASSTA JAMSSTRA MASTERS ANTREIDS ANTREIDS ANTREIDS ANTREIDS ANGESCHA ANGE
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70			AYOLATIO S AARTEISS BEZADON ABSSA44 BEZ189S1 14953433 AMSS259 ABSTOVA AZAPI ODIS NEDRES HTT795 ZHSEZTS ADEZTZS ABSSA55 BEF66965 REZZE ASAPESSEN WALH HTT7550 AMSS959 BEF6520 BEF6969 AARTEISZ AMSTS252 AMSS552 ABSSZ52 ABSSZ54 ABSZ525 ABSSZ54 ARZEISSE AAZOSSZ1 TIS418 F10594 DSSA49 ALDHT04Z T20449 AA41895T H45008 AW389735 (AW389737 AIZ42468 AA418749 AIZ13474 AAZZEISSE
75	111003 103240	14704022 3332_1	NG-2960 UPS191 MJ, D01008 XT01610 Z\$2578 L2900T EEESS194 AWYSZ023 AMYRDC13 AWXT5F 09 AL056S00 AAXS690 AAX354TZ AWZ690T1 BECRAEZE BECRST00 AWYSFLATT BESTSHOP1 Z8198 AAWXT5F XA WYSSF14 BECRST98 AWX5F2 AWX5F
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			A1253 126 A1399784 H30300 ANH69278 AN199471 AM50399 A1083994 A1926918 AM68955 A3006932 R60701 H3027391 A1639698 AVV250106 A177716 A1251175 A1091069 T32885 A.4.770382 ANN802933 AM682931 A1392999 A.7.777151 A1926386 AVV773202 A161291 Z41574 A1688604 A1825589 AVK690300 A1826622 AA346416
10	111157	47672_1	AL 109729 AI021970 AI033783 AVIZ92816 AA976653 AI343404 AI829907 AIZ48462 NG8085 AI682705 AA8449 11 AI014335 AA393642 AA676225 NG8613 AA370652 W90703 AA435680 AA985678 AW450047 AW966138 AI682668 AW473059 AA348132 NB0524 W90702 R00700
	134032	15436_1	NM_005025 ZB1325 R12152 A1133613 AA164563 AA115876 F07041 AA136450 R14666 Al817265 AW903276 AI805394 AA365992 AW959995 AA364817 AA364755 AI742453 AA873062 A1207467 AA165401 A1469568 AA588349 AI797921 AA912147 AA933058 N47859 A498633
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25			H00209 HTTPO1 AWRISTYS H00205 AMARESIA H7250F KRISSA MESSER ASSERVA ASSERVA AMARISTA AWRISTOZA MESSORS AWRISTOZA AWRISIOZA AWRISOZA ARTISTRA AMAZERIA AMARIOZA H7350 AMARISTA SA AWRISTOZA
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60	133473 102748	13028_3 8256_1	AW030199A (J005000) AW030195 AU00597A AD20899 AW030182 AW1720020 F77264 AW15099 A AU11712 F2 1009 A A202005 BED1813B AW04050 U79029 AW (100608 DE28) 8404 E007240 BED27360 BED
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20	134133	28210_1	AA32294 AUD78991 031598 ATROMTZ AL159078 EEZYTF95 F12693 F196964 R14494 AA359899 BE127004 AB313325 AB015991 X39320 MM, 001946 BE1270592 BE1277522 AA59986 R55030 AWS6084 BE3209045 AVS7942 AA31210 AVSF9570 BA459856 AV59587 BA45986 AV595877 AA354475 AA4595 B169598 F10695 B169598 F10694 F106730 B169598 F10673 B169598 F1067
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20			AW304745 AV657192 Al553650 AW118847 Al871278 BE075093 AI243817 BE046860 Al560849 Al669278 AA893608 N39152 AW131465 AA767854 Al457964 AA908227 AA719622 Z41372 T93491 AA964262 BES37965 T96329
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45		2210_15	RE205801 AIS97747 AA159574 AA610279 AI049R47 AA780111 AI016328 AI381296 AI672628 AI 197771 BE504554 AA252994 AI800528
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50			RE328570 N51129
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15			AA348340 AA018642
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80			A(038335 AA205790 AA918345 AIS36571 H46750 BE350087 AW197014 Z43666 A(080414 AA886382 H98215 A(202597 C15906 C15872 C88812 D60117 D63401 D81322 D62755 H19694 AA688395 C15901 C15411 AA683218 AA991302 A(263272 AV/469791 A/570417 A)114678
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			AA206963 H43859 N80428 H45366 H39083 AA425373 AA425465 AA846690 AA046580 D55145 AA621706 T07073 D54657 T08681 M78869

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5			T31625 (178559 W1671 H30034 AWG90851 AAMAD11 H60003 D11966 AWA66665 AWG26525 AW625215 AW56505 H50052 H60957 AA1 S269 AWG5055 AW667076 AWG706 AW67276 AA51015 AWG1060 AW69706 AW67765 A371558 (M65622 AW67765 AH10765 AW67676 AW6776 AW7676 AW6776 AW7676 AW6776 AW67
	105500	47391_1	AW620166 N2760T A4255695 AJ86416 Al42423 AA781512 AA898422 A4664242 H35603 AW339154 AW529590 AJ600160 AW513176 AW625866 AJ24191 A4224998 AW256485 CO1116 R80552 AJ850862 AA333630 AA856439 AW026325 W75647 AF085390 AJ267672 W74079 AZ76654 AJ420727 AJ344456 AZ96488 W60717 AA224927 AW20762 AJ868213 AW357102 H444430
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35	407700	47044	AA53398 AM188581 H85071 H85226 AA9786949 H85456 M725665 AA725465 H957071 A264415 A720572 A259416 W57715 AM194286 R95686 H85106 A0174855 AA918031 A1564659 AK78424 H14085 AW166317 AA775239 AA015626 AA472622 AA977888 Z38375 A1000910 A431380 AA524244
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50			C18724 U42404 AW378684 AW580570 BE174525 AA600101 AW750511 AI356556 AI750644 T47699 R81772 T49245 T93048 R36450 T49421 AW390369 AA082805 BE142984 AA129277 N83780 AI370335 H43251 AA30915 R23404 AA367947 AW608529 W25319 AA936923
	104933	6451_1	AMS/276 H 175533 R 15348 A 175047 177689 R 26212 T 25447 L 141890 I 14/2456 A N/547480 I V/5621 R 15/174 H 14112 A LOTEZY A WARBERS B 175047 D 165090 A M/27621 A 1435554 A M69604 0 1030 A M/57230 F 16504 A 165004 1 76687 8 I A455242 AMS4022 A REZ4405 A MY15070 8 M/22011 A 17612 29 A 1744400 A M/70707 A W/32013 R 14/1748 Z 14662270 A M69615 I OA 148091 A A515240 AMS5036 A A M/5090 A M/60000 A M/5071 A B 0/60509 R 16704 A 1610508 M 1/17600 E J 1680627 A M69604 A 0/67660 T 159044 A 176715 Z 14697/750 AMS5036 A A M/5090 A M/60000 A M/5071 A B 0/60509 R 167040 A 1610508 M 1/17600 E J 1680627 A 0/67600 A 0/67600 A 167040 A 167050 A 167060 A 167040 A 167050 A 167060 A 167040 A 167050 A 167060 A 167060 A 167040 A 167050 A 167060
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75	104986	128798_1	A-224/929 AVZ-505-8 AWC88826 AW293764 AA846265 AW771263 AIS34858 AI720358 AA 101632 AW161292 AIS69728 BE218525 AA779354 AI763721 AW244016 AIR02114 AIR69386 A428138 AW024280 F00967 AW026304 AI373133 AX35587 AI822852 W85852 R79192 AI61148
	120649	201075_1	ARRIZTHA AUGSSBO ARAZITSB AWGAZBO FILISBIY AWGABBA ALS/STSS AKSSBOR/ ABSZBSZ WIBBBSZ KY919Z ARFT1440 ARBT322 AA642329 AKGOTFO AUGS479 AA832416 AA807302 AA854015 AA889829 AW771843 AI60885 AI819500 AW663384 AA905058 AA287115 AW974422 AIS78463 AW302499
80	120655	37998_1	AA36599 A-161396 AA24960 AF11692 A153496 N39717 AA4699 ANKOZ105 ANKOZ1057 IEELESSO ANKOZ769 BE176728 BE176722 NNOC4755 ANKOZ25 ANKOZ64 M36964T AA27996 AA46978 AK7067T ANKOZ218 AX77233 A151440 BE17457 A169875 AA82751 AA36272 XA96224 ASSASTI AK869896 AA27347 ANKSSOS A186676 ACIESSI AAZ7647 A1688753 AA65925

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50	112902	22861_1	AL036633 F11794 F11783 H18042 T66089 H23079 R19493 AW134660 Al299437 AL133995 AA067405 N78357 AA917450 Al002692 T09262 T66008 H29290 Al200874 AA894415 Al732887 Al791768 Al733447 AA988785 N62128 T09261 AW956936
50	106350	29794_1	AKOD1404 ALDBO146 AW405449 AA38006 AA311866 AW246592 AA314336 A4,71604 EE255449 AA33868 NBE231 EE273256 AA131058 W21655 AB020981 EE255879 EE538183 AF020822 AMI,004701 AA446945 R2074 AA26634 AA129846 BE04788 AA1274A0 AA368440 AW356725 BE031899 EE12784 AU08642 AB88224 A1146662 A223319 AL66671 IA1869694 AW373217 BE073401 BE082200 AW1691 80
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	112941	4686_1	AW163034 NIM_004209 AJ002309 T06741 T80472 NM8923 R81887 BE313769 H20603 N46419 AW157065 H03872 AW291363 H03873 AA825164 AW104966 AA776642 A4989308 T16232 H20514 AA890072 AA878765 BE314664
5	105726	5801_1	NM_012058 AB02965 T71631 T67794 A344983 H46945 A191110 BEZ71163 AA513905 A451235 T67716 T71365 D3 1104 A1670551 AW029165 DE207319 A4161164 A4292228 A4815137 A4994765 A4191099 A4994766 N59773 A1000315 H46624 W56503 T64051 W56600 R0000 R00309 T86073 AW030226 A4465059 H27368 P690307 H55599 AW91750 A4714781 T73935 AW381810 AW501287 AW601284
			BE063948 AW601286 BE063943 BE064022 DE063949 BE063947 AV651606 BE063950 BE063954 AW501282 AA345127 AW601288 BE063945 AW322058 BE064024 AV653635 AW991637 AW393063 PS9239 A1658680 BE395604 N34330 H65944 AA495253 AI769302
10			AW675052 AW603131 BE467506 N25046 AW672383 AB71397 AA421049 AA179101 R71936 A 658506 AW005082 A1380622 A1499815
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15			AW241303 AA354617 AA455270 AK35593 A1208885 AA235760 AW859848 A1333957 AA292711 H13268 AA701078 R70764 AA767990 N53058 AAS95091 AI566574 R77646 D52194 AW770208 A1208878 AA382459 AA382328 AA587962 N50415 AA382442 AA382302 AA382393
	106390	7471_1	AJ297436 H02338 AA158880 N32011 N32614 AA526838 AA446964 A1677792 A1139699 AW205435 AA640913 A1685741 A1936226 A1094278 AA548812 A1810655 AA702913 A1017464 AA630584 A1597844 AA662112 H96372 AW338346 AA662018 AA543070 A1066213 AW973274
20			Al221540 Al685668 AW134915 Al696731 R08364 Al391510 Al220820 AA662861 Al623123 AW006591 Al392790 Al972502 AW139444
	129265	27030_11	A1686348 A1801281 A1683077 A1201402 A1674308 A1474807 AA888896 A1972562 NM_005672 AF043498 AA530892 R46439 R22993 W51996 NM_004417 X68277 AW013822 R68960 A1913774 AW014748 A1184379 AA459716 R22310 AA524040
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	106774	44046_3	Al216748 AA934429 AW135031 Al658617 Al686168 Al005676 AW275800 T79465 AW501146 R41671 Al989757 AA705657 T58684 Al265567 AW503040 AA478112 AW407946
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35	100154	16656_1	HIGHTON UNIFORM THAT, BIT 1789 BESIT/188 BESIGNES SESSION IT 26 EXTREME BESIGNES ANNO-MAIO ANNO-MAP BESIGNET SESSION BESIT/188 BESIGNED ANNO-MAIO
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30			AMMOSISP ACSTROM AMESSEG AMASZYA AMSZYCZA AMSZYCZA BERLIOSTA AMISCASKA AMASZYA TUZI YA MYTESSE WEZSEA HISANG UZ IRSA AMMOSISPA AMYSEK AMASZYA AMASZYA AMISCASKA AMISCASKA AMISCASKA AMASZYA SEZIELIZI AMASZYA
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10	100372	29155_1	NM, 014791 D79997 A3307070 AA438897 AA307476 AW0498325 AL135150 AA451253 AB99521 AA 829419 AJ508971 AA587220 AA903137 AW03353 A1870210 AA4620956 A1882492 AA744784 AA744782 W62362 AA768291 A1637653 A1838723 A1753377 AW134936 AA639599 AA664363
15	116024	17331_1	AABBRY AF2-KUTS AA/T2075 ABCSSEM AACTESS HAYDE SIN HA RIPTOS HAWT 188 AF1-6227 ABT 198 ABCRES HA HEBBO (1880) OF MADES AA AASSET HAT HEBBO (1892) OF HAT HEBBO (1892) ABCRES HAND ARE HAVE HAR HEBBO (1892) ABCRES HAVE HAD ARE HAVE HAVE HAVE HAVE HAVE HAVE HAVE HAV
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55	115414	173073_1	AA662240 AW769037 AW769660 AI913396 AA465182 AA214513 AW511261 AA283832 AI767608 AW510769 AW968608 AW967783 AA788028
33	108218 115471	107976_1 11801_1	W5750 A-057286 MY797200 AB972066 A-058711 AIR 4269 AK001376 DE38044 DE380687 DE489881 Al128092 Al780051 AI829784 AI810043 A-284708 AV752563 AI880487 A-86/6701 A-8829971 W59052 AI857405 A-8693657 A0003180 A-9514968 AV972449 A/754241 A-882580 AL121107 AI863791 AI837676 A/750708 AI022771
60	114877	58_20	AN22773 WWXTRS AZ24685 X146964 ARTG311 AX03026 AX78374 AX076856 AX77502A AX546902 AX55918 R55788 AX287138 AW117381 WXX24516 BEZZ502 AX252240 AX076340 AX462836 AX16740 AECS350F EZZ574 AA625094 AX2591 AX67691 AX2671 AX67691
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30	130567	2239_1	AASSIDE AATSIDE AATSID TIS MI JOOGHI LINGO ANKINDO AASSIDE ZAAGATS ANGIDOTA AKITTIS AI 161742, AAGSIDS EESSIGG AASSIT AIKANDOS AASSIGSA AAKSID ATTIN TO EGETA ARSIDS AATSIDS AASSIDS AATSID AAGSIDS AATSIGSA AASSID AATSID AASSID AATSID AASSID AATSID AASSID AATSID AASSID AATSID
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45	100569	27120_15	Z4/1788 WIN-1469 AUXC2916 AV4456/13 AVX093549 ÄVK065269 F05032 A/20520Y ÄVV027964 R58950 N7-4344 W80733 C01142 R38054 R31867 H786115 R80066 AUXT274 R72558 AUXT274 R72558 AVX5432 AVX542 R410 AVX544
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30	331517	288032_1	A1346671 A1337560 T96138 A1128634 A1738989 A1738907 AA026199 AA089670 AA026503 A1675681 A1355934 ANVIG6892 A1569925 AA767454 AA9614394 AA730044 ANVIYO292 N49610 A1341962 A1683402 AA424064 N23063 N23099 N38889 A1627246 ANVISS949 A1281421 AA708232 ANVIFF603
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20			AW750034 BE072537 BE297947 AW732361 AA449336 D29574
	332732	5436_1	AF191019 NM_015516 BE546494 AL110276 R13844 BE313586 BE336912 R18704 R18703 AA045868 T70952 BE336901 T60387 BE149749 BE271848 BE271902 AA489929 Z45402 T64360 AA305745 AA009451 T95706 H14907 AA299901 C03221 T72431 AW471185 AA335297
			BEZ/1848 BEZ/1902 AA469529 245402 154360 AA30545 AA005451 195/05 H14907 AA269901 QUSZZ1 172431 AW4/1185 AA336297 AJ269100 AA345072 AW965160 H27581 R48910 H25380 AA335281 AW973283 T79590 AW183447 T64172 AJ744097 AJ342358 AA336102
	*		AZSS100 AASSC072 AWSC0160 HZ/501 KW0910 HZ0500 AASSC01 AWS75203 175050 AW160447 164172 A/744097 A/54236 AASSC102 AA335299 BE208375 AI140834 AA688181 AI860314 AI738613 T70902 R42077 AI884558 AA489798 AI130828 AA009735 H25381 AW612425
25			R48901 H27507 H30105 H4671 Al631362 AA558470 AW014412 AA550059 AA46501 AW389435 Al039657 H14514 AA974256 R42078
23			A/2457/8 T61896 AH592702 A07/4139 AB17313 A)041484 AA437138 A)613032 A147/891 A)447/945 AW1977727 A)07/4399 A)7/58636 A1598048
			A972077 M65390 B36999 R71936 A967492 T40081 Z41115 AA772775 T41013 A695691 T40096 A8228822 N93464 AV955524 AA088651

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TABLE 1C

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Pier: Listique rember corresponding to an Eos problese!
Rel: Sequence source. The 7 dig in minbers in this column are Genhard Montfaire (G) numbers. "Dunhamil, et al." refers to the publication entitied "The DNA sequence of human chromotomy." Columnia to al. (1998) bitters 047-048-048.
Strand: Indicates DNA stread than which soom were predicted.
The Colonia incidents in client of the colonia was predicted and an account of the colonia of

	Pkey	Ref	Strand	Nt_position
10	332792	Dunham, I. et.al.	Plus	73381-73768
	333135	Dunham, t. et.al.	Plus	3361208-3361369
	333137	Dunham, it et al.	Plus	3367643-3367726
	333138	Dunham, I. et.al.	Plus	3369205-3369323
	333139	Dunham, I. et.al.	Plus	3369495-3369571
15	333516	Dunham, I, et.al.	Plus	5570204-5570390
	333517	Dunham, I. et.al.	Plus	5570729-5570925
	333795	Dunham, I, et.al.	Plus	7807688-7807795
	333796	Dunham, I, et.al.	Plus	7808253-7808319
	333808	Dunham, I. et.a.	Ples	7880600-7880775
20	333809	Dunham, I. et.al.	Plus	7880600-7880775
	333845	Dunham, I, et.al.	Plus	8005832-8005945
	333849	Dunham, I, et.al.	Plus	8018323-8018472
	334101	Dunham, I. et.al.	Plus	9973413-9973550
	334616	Dunham, I. at.al.	Plus	15176123-15176470
25	334891	Dunham, I. et.al.	Plus	19299770-19299944
	334899	Dunham, I. et.al.	Plus	19315168-19315311
	334900	Dunham, I. et.al.	Plus	19315678-19315743
	334902	Dunham, I, et.al.	Plus	19317083-19317195
	334905	Dunham, I. st.al.	Plus	19322553-19322680
30	334906	Dunham, k et.al	Plus	19323493-19323590
50	335044	Dunham, I. et.al.	Plus	20842088-20842682
	335149	Dunham, I. et.al.	Plus	21497441-21497587
	335809	Dunham, I. et.al.	Plus	26310772-26310909
	335810	Dunham, I. et.al.	Plus	26314767-26314849
35	335824	Dunham, I. et.al.	Plus	26376860-26376942
33	336054	Dunham, I. et.al.	Plus	29161685-29161937
	336721	Dunham, I. et.al.	Plus	3371522-3371586
				23934889-23934962
	337182 337674	Dunham, I. et.al.	Plus Plus	3332616-3332697
40		Dunham, I. et.al.	Plus	3332010-3332097
40	337675	Dunham, I. et.al.		3335368-3335505
	337755	Dunham, I. et.al.	Plus	3971764-3971900
	338038 338316	Dunham, I. et al.	Plus	8138219-8138392
		Dunham, I. et.al.	Plus	17089711-17089988
45	333124	Dunham, Let.al.	Afnus	3318017-3317932
+3	333743	Dunham, I. et.al.	Minus	7573218-7573060 12730944-12730387
	334221 334222	Dunham, I. ot.al.	Afnus	12732417-12732289
	334282	Dunham, I. et.al. Dunham, I. et.al.	Minus Minus	13285293-13285178
	334502			14488605-14488526
50	334578	Dunham, I. et.al. Dunham, I. et.al.	Minus	15004462-15004304
50	334951	Dunham, I, et.al.	Africa Minus	20147708-20147502
	335269		Mnus	22305950-22305708
		Dunham, I. et.al.		
	335290	Durinam, I. et.al.	Minus	22309950-22309891
55	335293	Durham, Letal.	Minus	22316408-22316275
22	335682	Dunham, Letal	Minus	25421215-25421093
	335753	Dunham, Letal	Minus	25761535-25761444
	335755	Dunham, I. et al.	Minus	25763806-25763747
	335756	Dunham, Letal.	Minus	25764330-25764251
60	336662	Dunham, Let.et.	Minus	2158060-2157993
00	336684	Dunham, L et.al.	Minus	2158060-2157993
	337603	Dunham, I. et.al.	Minus	1299296-1299194
	338561	Dunham, I. et.al	Minus	22311966-22311856
	338562	Dunitam, f. et.al.	Minus .	22312594-22312465
10	339186	Dunham, f. et.al.	Minus	32339211-32339097
65	325889	5867087	Plus	223829-223891
	330032	6682596	Plus	85177-85237
	330033	6682596	Plus	96663-96723
	326213	5867224	Minus	60751-60927
70	326816	6552458	Plus	198354-198436
70	327110	6117842	Plus	94608-94785
	327821	5967968	Plus	131060-131232
	328164	5868068	Minus	27080-27226
	328648	6004473	Plus	424829-424959
75	329365	5868838	Minus	107687-107765
13				

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- Table 2 his down 1165 games anticold bit our on thereding operation, pations driving antidogen withdrawed of protectic cornor factors. Those groces were exhibited by any patient of the protection of the protect
- (hi-lo-lo-hi pattern in table 2A), 2. Genes filled are expressed early in the time course, then drop off in expression immediately after androgen-withdrawal, and do not express again with emergence of androgenindependence (hi-lo-lo-lo pattern in table 2A).
- 3. Genes that are expressed early in the time course, then drop off in expression after several days of androgen withdrawal, and do not express again with emergence of
- 10 androgen-independence (hi-hi-lo-lo pattern in table 2A).
 - Genes that are not expressed early in the time course, but express only with emergence of androgen-independence (lo-to-to-th) pattern in table 2A.
 Genes that are not expressed early in the time course, but then express as androgen is withdrawn and continue to express with emergence of androgen-independence (lo-to-to-th). hi-hi nattern in table 2A).
- 6. Genes that are not expressed early in the time course, but then express as androgen is withdrawn and drop off again with emergence of androgen independence (lo-lo-li-lo 15 pattern in table 2A).
- Table 28 lists accession numbers for primeleys lacking a uniquenel D in table 2A. For each probeset is listed a gone cluster number from which disjonant-policies were designed. Game clustes were complied using sequences derinder from Genicalit ESTs and mRIVAX. These sequences user a clustered based on sequence similarly using Clustering and Afformed Tools (Double' wid., Oldstind California). Genius accession numbers for sequences complied good holds are gled in the "Apposited for th
- 20 Table 2C lists genomic positioning for primakeys lacking unique ID's and accession numbers in table 2A. For each predicted exon is fisted genomic sequence source used for prediction. Nucleotide logations of each prediction are also listed.
- TABLE 2A: ABOUT 1165 GENES SELECTED TO HAVE AN INTERESTING EXPRESSION PATTERN DURING ANDROGEN WITHDRAWAL OF PROSTATE CANCER
 - Pkey: Unique Eos probeset Identifier number ExAcon: Exempler Accession number, Genbank accession number
 - UnigenelD: Unigene number
- 30 Unigene Title: Unigene gene title Peltern: Broadly defined expression pelterns during androgen withdrawal

	Pkey	ExAcen	UnigenelD	Unigene Title	Pattern
	433412	AV653729	Hs.8185	CGI-44 protein; sulfide dehydrogenase li	lo-lo-hi-lo
35	429097	AK001270	Hs.196066	hypothetical protein FLJ10408	lo-lo-hi-lo
	442731	Al868167	Hs.131044	ESTs	lo-lo-hi-lo
	420820	W26096	Hs.336635	Homo sapiens, clone IMAGE:4179482, mRNA	lo-lo-hi-lo
	422267	AB033044	Hs.114012	KIAA1218 prolein	lo-lo-hi-to
	416953	N31537	Hs.269046	ESTs .	lo-lo-hi-lo
40	413277	H24177	Hs.75262	cathensin O	io-lo-hi-lo
	410209	AJ583661	Hs.60548	hypothetical prolein PRO1635	lo-lo-hi-lo
	428523	AW974540	Hs.98526	ESTs	lo-lo-hi-lo
	435847	W93821	Hs.39780	CDA017 protein	lo-lo-hi-lo
	443967	AW294013	Hs.200942	ESTs	lo-lo-hi-lo
45	440638	AA907075	Hs.131307	ESTs	lo-lo-hi-fo
	404054			Target Exon	lo-lo-hi-lo
	431697	H96740	Hs.38540	ESTs, Weakly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo
	432114	AL036021	Hs.8934	ESTs	lo-lo-hi-lo
	446397	AW275603	Hs.200712	ESTs	lo-lo-lti-lo
50	414094	H15088	Hs.31433	ESTs	lo-lo-ht-lo
	424005	AB033041	Hs.137507	veng (van gogh, Drosophile)-like 2	lo-lo-hi-lo
	424401	H67220	Hs.169581	death effector domain-containing	lo-lo-hi-to
	449749	AJ668611	Hs.49760	ESTs	lo-lo-hi-lo
	458368	BE504731	Hs.138827	ESTs	lo-lo-hi-lo
55	427221	L15409	Hs.174007	von Hippel-Lindau syndrome	lo-lo-ht-lo
	432715	AA247152	Hs.200483	ESTs, Weakly similar to KIAA1074 protein	lo-lo-hi-lo
	425980	AA356951		gis:EST77963 Pancreas tumor III Homo sapi	io-lo-hi-lo
	412492	AW962604		glxEST374677 MAGE resequences, MAGG Homo	lo-lo-hi-to
	438882	AA827695		glxod56c02.s1 NCI_CGAP_GCB1 Homo sepiens	lo-lo-hi-lo
60	422473	U94780	Hs.117242	meningioma expressed antigen 6 (collect-c	lo-lo-hi-lo
	404211			NM_005936:Homo sapiens myeloid/lymphold	- lo-lo-hi-lo
	423019	A)640185	Hs.283626	ESTs	10-lo-ls1-10
	443559	A)076765	Hs. 269899	ESTs, Moderalely similar to ALU8_HUMAN A	lo-lo-hi-lo
00	444291	Al598022	Hs.193989	TAR DNA binding protein	lo-lo-hi-lo
65	428065	A)634046	Hs.157313	ESTs	lo-lo-hi-lo
	442566	R37337	Hs.12111	ESTs	lo-lo-hi-lo
	442202	BE272862	Hs.106534	hypothetical protein FLJ22625	lo-lo-lil-lo
	439456	A)752409	Hs.109314	hypothetical protein FLJ20980	lo-lo-hi-lo
70	423476	AL035633		Human DNA sequence from clone RP5-1046G1	lo-lo-hi-lo
70	437952	D63209	Hs.5944	solute carrier family 11 (proton-coupled	lo-lo-hi-lo
	451987	AA815092	Hs.77554	Homo sapiens cDNA FLJ14967 fis, clone TH	lo-lo-hi-lo
	453408	A)804732	Hs.295963	ESTs	lo-lo-hi-to
	444004	N39842	Hs.301444	KIAA1673	lo-lo-lti-lo
7.0	452691	AA164842	Hs.192619	KIAA1600 protein	lo-lo-hi-lo
75	434865	AW060449	Hs.116507	ESTs	io-lo-hi-to
	440819	AJ809444	Hs.202108	ESTs	lo-lo-lti-lo
	419526	A)821895	Hs.193481	ESTs	. lo-lo-hi-lo
	422072	AB018255	Hs.111138	KIAA0712 gene product	lo-lo-hi-to
80	453459	BE047032	Hs. 257789	ESTs	lo-lo-hi-lo
٥U	419038	AW134924	Hs.190325	ESTs	lo-lo-hi-lo
	413243	AA769266	Hs.193657	ESTs	lo-lo-lii-lo
	432079	AW972746		gb:EST384840 MAGE resequences, MAGL Homo	lo-lo-lai-lo

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441328 Al982794 Hs.159473 ESTs InJohido R39769 416508 ESTs. Moderately similar to ALUS HUMAN A lalahida 451066 AI758660 Hs.206132 lo-lo-hi-lo 446017 N96238 ESTs He 55185 5 Homo sapiens cDNA FLJ 13 162 fis, clone NT 447104 Hs.210706 lo-lo-hi-fo KIAA1554 prolein Al 161961 Hs 17767 447211 InJohido 447765 AW014112 Hs 161390 FSTs Indo-hida glxEST02297 Fetal brain, Stratagene (cat. 429540 M85776 loJo-hi-lo gb:ow76b09.s1 Soares_felal_liver_spleen_ 444314 A1140497 lo-lo-hi-lo 10 414555 N98569 Hs.76422 phospholipase A2, group IIA (platetels, UDP-N-acetyl-alpha-D-galactosamine:polyp lo-lo-hi-lo 432677 NM_004482 Hs.278611 Al906339 Hs.97927 422091 ESTs lo-lo-h1-lo gb;yu86c02.rt Soares folgi liver spleen H90946 423028 In-in-hillo AF204231 Hs.182982 444040 addin.67 la.la.hi.la gague. ESTs 15 441111 AI806867 Hs.126594 lo-lo-hì-lo 418838 AW385224 Hs.35198 eclonocloofide pyrophosphalase/phosphodi lo-lo-hi-lo 415999 AA172179 Hs.294029 ESTs lo-lo-hi-lo ATP-binding cassette, sub-family A (ABC1 Homo sapiens clone 23664 and 23905 mRNA 429615 AF258627 He 211562 lo-lo-hillo 427774 44278583 He 180737 h.h.hih 20 AA811371 438685 He 123362 FSTs lo-lo-hi-lo 424776 AJ867931 Hs.164595 ESTs lo-lo-hi-lo 413786 AW613780 Hs.13500 ESTS lo-lo-hi-lo 421077 AK000061 Hs.101590 hypothetical protein 445837 AI261700 He 145544 lo-lo-hi-lo 25 Homo saviens cDNA FLJ13555 fis, clone PL 449282 AT DARDER He 23437 lo-lo-hi-lo Homo sepiens cDNA FLJ13580 fis, clone PL 414065 AW415373 He 271240 ladabida 43252 AW975028 Hs.102754 FCTe hulo-hUh 412093 BE242691 Hs.14947 **ESTs** lo-lo-hi-lo 457121 AJ743770 Hs.180513 ESTs. Weakly similar to KIAA0822 protein lo-lo-hi-lo 30 417280 AW173116 Hs.250103 ESTs lo-lo-h1-lo AB002438 Hs.29596 Homo sapiene mRNA from chromosome 5021-2 452445 lo-lo-hHo 438624 44889055 Hs.123466 **FRTe** hihhh AA992480 Hs.129874 ESTs 442343 loviorbillo C14000338*:gij7459502|pirj|\$74665 outer calcineurin-binding protein calcarcin-1 lo-lo-hi-lo 401416 35 437176 AW176909 Hs.42346 Al872360 Hs.209293 lo-lo-hi-lo 451863 ESTs lo-lo-hi-lo AW137268 Hs.270954 449295 FSTe loubillo 42684B H72531 He 36100 EST₀ Induktion ESTs. Weakly similar to ALU4_HUMAN ALU S 445467 Al239632 He 15617 lo-lo-hi-lo 40 418662 Al601098 Hs.151500 ESTS Injuhilo 416239 AL038450 He ARGAR ESTe lo-lo-hi-lo 428054 Al948688 Hs.288619 ESTs 435284 44879470 He 96849 Homo sepiens cDNA FLJ11492 fis, clone HE lo-lo-hi-lo Hs 101615 FRTs 424332 AA338919 Indubido 45 442369 A1565071 He 159983 FSTe Industria. 420717 AA284447 He 271887 ESTs Indubido 439584 AA838114 Hs.221612 ESTs lo-lo-hi-lo 440260 AI972867 lo-lo-hi-lo He 7130 copine IV 426269 H15302 Hs.168960 Homo sepiens mRNA; cDNA DKFZp566A1046 (f lo-lo-hi-le 50 428398 AJ249368 His GRASS FRTs Indiahida Homo sepiens breast cencer antigen NY-BR ectonucleotide pyrophosphatase/phosphodi PTPL1-associated RhoGAP 1 He 326736 407276 AI951118 lododido 409339 AB020686 He 54037 lo-lo-hi-lo 442150 Al368158 Hs.70983 lo-lo-hi-lo 415787 H01463 Hs.93534 FSTe 55 430685 A1690234 Hs.191666 ESTs, Weakly similar to GNMSLL retrovtru lo-lo-hi-lo lo-lo-hi-lo 443794 N94104 He 29280 **ESTs** ES13 SH3 domein binding glutamic acid-rich pr microtubule-associated protein 2 gb:601503815F1 NH_MGC_71 Homo sapiens c ENSP00000226812*:KIAA1494 protein (Fragm AWR21329 Hs.14368 446215 Indichido NM_002374 Hs.167 BE614061 441285 lo.lo.bi.lo 448738 Indichido 60 403746 lo-lo-hi-lo R18374 Hs.117956 ESTs 434022 435714 AA699325 Hs.269680 ESTS lo.lo.hi.lo gb:EST391359 MAGE resequences, MAGP Homo gb:EST14192 Testis tumor Homo sapiens cD Homo sapiens clone TCCCTA00151 mRNA sequ lo-lo-hi-lo 439848 AM979249 421074 44301270 lo-lo-hi-lo 65 433333 Al367347 Hs.44898 lo-lo-hi-lo 449919 Al674685 Hs.200141 ESTs lo-lo-hi-lo AA609200 gb:af12e02.s1 Soares_lestis_NHT Homo sap Homo sapters cDNA FLJ12381 fis, clone MA lo-lo-hi-lo 407192 AA888311 Hs.17602 436169 lo.lo.hl.k 418824 Al734080 Hs.104211 ESTs lo-lo-hi-lo 70 432432 44541323 He 115831 ESTe (n.ln.hi.ln 426172 AA371307 Hs.125056 FSTs in-in-hi-in C12000586*:gij\$330167]dbjjBAA86477.1| (A sema domain, immunoalobulin domain (lg), 401093 io-lo-hi-lo 426716 NM_006379 Hs.171921 lo-lo-hì-lo 439569 AW602166 Hs.222399 CEGP1 prolein lo-lo-hi-lo 75 AW970965 Hs.290653 ESTs 451720 lo-lo-hi-lo 44554766 gb:am20a10.s1 Soares_NFL_T_GBC_S1 Homo s A29163 in.ln.hi.in Hs.262070 ESTs BE218886 lo-lo-hi-lo 432435 408170 AW204516 Hs.31835 ESTs lo-lo-hi-lo 433530 BE349534 Hs.281789 ESTs lo-lo-hi-lo 80 425776 U25128 Hs. 159499 parathyroid hormone receptor 2 lo-lo-hì-lo 430088 AA464964 spaces over lumor NbHOT H 422725 AA315703 Hs.199993 ESTs, Wealdy similar to ALUB_HUMAN ## lo-lo-hl-lo lo.lo.hi.lo

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	432314	AA533447	Hs.312969	ESTs	lo-lo-hi-lo
	434609	R76593		gb.yi60c11.r1 Soares placenta Nb2HP Homo	lo-lo-hi-lo
	448760 417381	AA313825 AF164142	Hs.21941 Hs.82042	ADO36 prolein	lo-lo-hi-lo lo-lo-hi-lo
5	456334	T50392	Hs.271745	solute carrier family 23 (nucleobase tra FSTs	lo-lo-hi-lo
	435445	AA737345	Hs.294041	ESTS	lo-lo-hl-lo
	411928	AA888624	Hs.197289	rab3 GTPase-activating protein, non-cata	lo-lo-hi-lo
	438869 423932	AF075009 T95633	Hs.189703	gbtHomo sapiens full length insert cDNA FSTs	lo-lo-hi-lo lo-lo-hi-lo
10	422222	A)699372	Hs.193247	hypothetical prolein DKFZp434A171	10-10-11-10 10-10-hi-10
10	434941	AW073202	Hs.334825	Homo sapiens cDNA FLJ14752 fis, clone NT	lo-lo-hi-lo
	415736	AA827082	Hs.291872	ESTs	lo-lo-hi-lo
	432722	AA830532	Hs.326150	ESTs	lo-lo-hi-lo
15	435511 432242	AA683336 AW022715	Hs.189046 Hs.162160	ESTs . Weakly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo lo-lo-hi-lo
	451141	AW772713	Hs.247186	FSTs	lo-lo-hi-lo
	450546	AA010200	Hs.175551	ESTs	lo-lo-hi-lo
	413351	BE086815		ESTs	lo-lo-hì-lo
20	439324 452688	AF086134 AA721140	Hs.94309 Hs.49930	ESTs	lo-lo-hi-lo lo-lo-hi-lo
20	415669	NM_005025		ESTs, Weakly similar to putative p150 [H serine (or cysteine) proteinase inhibito	10-10-111-10 10-10-111-10
	450164	Al239923	Hs.63931	FSTs	lo-lo-hi-lo
	417169	R13550	Hs.246773	ESTs	lo-io-hi-lo
25	443645	R36475	Hs.24321	Homo saplens cDNA FLJ12028 fis, clone HE	lo-lo-hHo
25	424878 449618	H57111 Al076459	Hs.221132	ESTs	lo-lo-hi-lo lo-lo-hi-lo
	432572	Al660840	Hs.15978 Hs.191202	KIAA1272 protein ESTs, Weakly similar to ALUE_HUMAN IIII	lo-lo-hi-lo
	400293	N51002	Hs,306480	Homo saplens mRNA; cDNA DKFZp761E2112 (f	10-io-hi-lo
••	431474	AL133990	Hs.190642	CEGP1 protein	lo-lo-hi-lo
30	421674	T10707	Hs.296355	hypothetical protein FLJ23138	lo-io-hi-io
	438494 425332	AA908678 AA633306	Hs.130183 Hs.127279	ESTs ESTs	lo-lo-hi-lo lo-lo-hi-lo
	451411	AA017492	Hs.135655	FST	lo-lo-hi-lo
	419972	AL041465	Hs.182982	golgin-67	lo-lo-hi-lo
35	434804	AA649530	Hs.348148	gb:ns44f05.s1 NCI_CGAP_AN1 Homo saplens	lo-lo-hi-lo
	442832	AW206560	Hs.253569	ESTs	lo-lo-N-lo
	408660 432674	AA525775 AA641092	Hs.257339	ESTs, Moderately similar to PC4259 ferri ESTs, Weakly similar to 138022 hypotheti	lo-lo-hi-lo
	448150	AM72167	119-201333	ESTs, Weavily strike to 100022 hypomen	lo-lo-hi-lo
40	450466	AW379075	Hs.141742	Homo sapiens cDNA FLJ12211 fis, clone MA	o-lo-hi-lo
	452874	AK001061	Hs.30925	hypothetical protein FLJ10199	lo-lo-hi-lo
	412088	Al689496	Hs.108932	ESTs	lo-lo-hi-lo
	443451 453653	Al057404 AL040600	Hs.58696 Hs.188083	ESTs ESTs	lo-lo-hi-lo lo-lo-hi-lo
45	419863	AW952691	Hs.93485	Homo saplens mRNA; cDNA DKFZp761D191 (fr	10-lo-hi-lo
	420729	AW964897	Hs.290825	ESTs .	io-io-hi-lo
	440801	AA906366	Hs.190535	ESTs	lo-lo-hi-lo
	407284 428279	AJ539227 AA425310	Hs.214039 Hs.155766	hypothetical protein FLJ23556 ESTs, Wealdy similar to A47582 B-cell gr	io-lo-lif-lo lo-io-lii-lo
50	436862	Al821940	1101100700	ESTs, Moderately similar to ALUS_HUMAN A	lo-lo-hi-lo
	432340	AA534222		gb:rj21d02s1 NCI_CGAP_AA1 Homo sapiens	lo-lo-hi-lo
	442048	AA974603		gb:op34f05.s1 Soares_NFL_T_GBC_S1 Homo s	lo-lo-hi-lo
	418781 450642	T41160 R39773	Hs.8404 Hs.7130	ESTs	lo-lo-hi-lo lo-io-hi-lo
55	451661	AB020650	Hs./130 Hs.26777	copine IV Homo saplens, Similar to KIAA8643 protei	10-10-11-10
00	435812	AA700439	Hs.188490	ESTs	lo-io-hi-lo
	448065	AI459177	Hs.172759	ESTs, Moderately similar to ALU7_HUMAN A	io-lo-hi-lo
	453486	AL039201	Hs.173554	ubiquinol-cytochrome c reductase core pr	lo-io-hi-lo
60	414312 438980	AA155694 AW502384	Hs.191060	ESTs gb:UI-HF-BR0p-sks-f-12-0-UI.r1 NIH_MGC_5	io-io-hi-io Io-io-hi-io
00	408001	AA046458	Hs.95296	ESTs	lo-lo-hi-lo
	421476	AW953805	Hs.21887	ESTs	io-io-hi-io
	414426	D60745	Hs.25925	Homo saplens, clone MGC:15393, mRNA, com	lo-lo-hi-lo
65	444563 418771	N57057 AA807881	Hs.284163 Hs.25329	ANKHZN protein	lo-lo-hi-lo lo-lo-hi-lo
0.5	417843	W07361	Hs.22545	Homo sapiens cDNA FLJ12935 fis, clone NT	lo-lo-hi-lo
	415565	AA642449	Hs.48994	ESTs, Weakly similar to AF151800 1 CGI-4	lo-lo-hi-lo
	419229	Al827237	Hs.282884	ESTs	lo-lo-hi-lo
70	419905	AW248229	Hs.93659	protein disulfide isomerase related prot	lo-io-hi-lo
70	452870 449059	AW602761 AK000566	Hs.30909 Hs.98135	KIAA0430 gene product hypothetical protein FLJ20559	lo-lo-hi-lo lo-lo-hi-lo
	416157	NM_003243		transforming growth factor, beta recepto	lo-lo-hi-lo
	439305	AW393883	Hs.98968	hypothetical protein FLJ23058	lo-io-hi-lo
75	419235	AW470411	Hs.288433	neurotrimin	lo-lo-hi-lo
75	416640	BE262478	Hs.79404	neuron-specific protein	lo-io-hi-io
	434938 408177	AW500718 AI241733	Hs.8115 Hs.43871	Homo saplers, clone MGC:16169, mRNA, com ESTs	lo-lo-hi-lo lo-lo-hi-lo
	438459	T49300	Hs.35304	Homo sapiens cDNA FLJ13655 fis, clone PL	lo-lo-hi-lo
00	418381	AA682353	Hs.119237	ESTs	lo-lo-hi-lo
80	432161	AK000400	Hs.341181	ESTs, Weakly similar to envelope [H.sapl	lo-io-hi-lo
	418283 421443	S79895 BE550141	Hs.83942 Hs.156148	cathepsin K (pycnodysostosis) hypothetical protein FLJ13231	lo-lo-hi-lo lo-lo-hi-lo
	+21443	D2000141	1 10.100 148	ng poniveses protess FLM 1929 I	10-10-11HD

	416619	AF013168	Hs.79393	luberous scierosis 1	io-lo-hi-lo
	449802	AW901804	Hs.23984	hypothetical protein FLJ20147	lo-lo-m-lo
	446714	W73818	Hs.110028	ESTs 42 formation to	lo-lo-hi-lo
5	413195	AA127382 W52448	Hs.22404 Hs.56147	protease, serine, 12 (neurotrypsin, moto ESTs	io-lo-hi-lo io-lo-hi-lo
,	416051	AA835868	Hs.25253	mannosidase, alpha, class 1A, member 1	lo-lo-hi-lo
	438855	AW946276	Hs.6441	Home sapiens mRNA; cDNA DKFZp586J021 (ir	lo-lo-hi-lo
	425907	AA365752	Hs.155965	ESTs	lo-lo-hi-lo
	451295	Al557212	Hs.17132	ESTs, Moderately similar to 154374 gene	io-lo-hi-lo
10	415443	T07353	Hs.7948	ESTs	io-lo-hì-lo
	422366	T83882	Hs.97927	ESTs	lo-lo-hi-lo
	435163	AA668884	Hs.19155	ESTs	io-lo-hi-lo
	426559 448988	AB001914	Hs.170414	paired basic amino acid cleaving system	ko-fo-hi-fo
15	453655	Y09763 AW960427	Hs.22785 Hs.342874	gerrma-aminobutyric acid (GABA) A recepto transforming growth factor, bela recepto	ko-lo-hi-lo ko-lo-hi-lo
13	414516	Al307802	Hs.135560	ESTs, Weekly similar to T43458 hypotheti	10-10-111-10 10-10-hi-10
	420028	AB014680	Hs.8786	carbohydrate (N-acetylglucosamine-6-O) s	lo-lo-iti-lo
	430223	NM 002514		nechrobiasioma overexpressed gene	lo-lo-hi-lo
	425887	AL049443	Hs.161283	Homo sapiens mRNA; cDNA DKFZp586N2020 (f	lo-lo-hi-lo
20	442577	AA292998	Hs.163900	ESTs	lo-lo-hi-lo
	424940	AA985308	Hs.283902	ESTS	ko-lo-hi-lo
	428839	Al767756	Hs.82302	Home sapions cDNA FLJ14814 fis, clone NT	ko-lo-hi-lo
	443868 430334	W88483 Al824719	Hs.293650 Hs.328700	Home sapiens mRNA for RGPR-p117, complet ESTs	io-lo-hi-lo lo-lo-hi-lo
25	439686	W40445	Hs.235867	ESTs, Weakly similar to 138022 hypotheti	lo-to-tii-to
	423754	NM_016181	Hs.132526	melanoma anligen	ko-lo-hi-lo
	415205	H71616	Hs.135233	ESTs	lo-lo-lui-lo
	426413	AA377823		gb:EST90905 Synovial sercoma Homo sapien	lo-lo-hi-lo
••	407204	R41933	Hs.140237	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi-lo
30	430234	N29317	Hs.236463	KIAA1238 prolein	lo-lo-hi-lo
	437143	AW204056	Hs.8917	ESTs	lo-lo-hi-hi
	445162	AB011131	Hs.12376	piccolo (presynaplic cylomatrix protein)	lo-lo-hi-hi
	415083 442924	A/632683 AA533513	Hs.27179 Hs.93659	Homo sapieris cDNA FLJ12933 fis, clone NT protein disulfide isomerase related prot	io-lo-hi-hi lo-lo-hi-hi
35	429536	AA873016	Hs.206097	oncogene TC21	lo-lo-hi-hi
55	458584	AF217518	Hs.324136	PTD012 prolein	lo-lo-hi-hi
	419647	AA348947	Hs.91816	hypothetical protein	lo-io-hl-hi
	427201	AB037860	Hs.173933	nuclear factor I/A	lo-lo-ini-hi
40	428030	AI915228	Hs.11493	Home sapiens cDNA FLJ13536 fis, clone PL	lo-lo-ini-hi
40	411779	AA292811	Hs.72050	non-metastalic cells 5, protein expresse	lo-lo-hI-hi
	442482	NM_014039	Hs.8360	PTD012 prolein	io-lo-ini-hi
	417458 438021	NM_005655 AV653790	Hs.324275	TGFB inducible early growth response	lo-lo-hi-hi
	438021	D11928	Hs.324270 Hs.76845	WW domain-containing protein 1 phosphoserine phosphalase-like	lo-lo-hi-hi lo-lo-hi-hi
45	440676	NM_004987		LIM and senescent cell antigon-like doma	lo-lo-hi-hi
	421437	AW821252	Hs.104336	hypothetical protein	lo-lo-hi-hi
	456362	AW973003	Hs.179909	hypothetical protein FLJ22995	lo-lo-hì-hi
	407686	AW901268	Hs.126043	chromosome 21 open reading frame 51	lo-lo-hi-hi
50	431129	AL137751	Hs. 263671	Homo saplens mRNA; cDNA DKFZp43410812 (f	lo-lo-hi-hi
30	431874	AW610031	Hs.323914	translocase of inner millochondrial membr	lo-lo-hi-hi
	448072 436860	AM59306 H12751	Hs.24908 Hs.5327	ESTs PRO1914 protein	lo-lo-hi-hi lo-lo-hi-hi
	448770	AA326683	Hs.21992	likely ortholog of mouse variant polyade	lo-lo-hi-hi
	428044	AA093322	Hs.301404	RNA binding motif protein 3	lo-lo-hi-hi
55	451468	AW503398	Hs.293663	ESTs, Moderately similar to 138022 hypot	lo-lo-hi-hi
	440278	BE560870	Hs.9052	ESTs. Weakly similar to 2004399A chromos	lo-lo-hl-hi
	441102	AA973905		intermediate filament protein syncollin	lo-lo-hi-hi
	423942	AF209704	Hs.135723	glycolipid transfer protein	lo-lo-hi-hi
60	425254	U91985	Hs.105658	DNA fragmentation factor, 45 kD, alpha p	lo-lo-iri-hi
UU	409324 431707	W76202 R21326	Hs.343812 Hs.267905	lipoic acid synlhetase hypothetical protein FLJ 10422	lo-lo-hi-hi lo-lo-hi-hi
	423335	AB018337	Hs.127287	KIAA0794 protein	lo-lo-hi-hi
	429200	AA447871	Hs.194215	ESTs, Weakly similar to I36022 hypotheti	lo-lo-hi-hi
	429898	AW117322	Hs.42366	ESTs	lo-lo-hì-hi
65	409604	AW44448	Hs.49124	ESTs	lo-lo-hi-hi
	431797	BE169641	Hs.270134	hypothetical protein FLJ20290	lo-lo-hi-hi
	437576	BE514383		prothymosin, alpha (gene sequence 28)	lo-lo-hi-hi
	415992	C05837	Hs.145907	hypothetical protein FLJ 13593	lo lo hi hi
70	458537 417665	W24704 AW852858	Hs.54773 Hs.22862	ESTs ESTs	lo-lo-hi-hi Io-lo-hi-hi
70	422292	Al815733	Hs.114360	transforming growth factor beta-stimulal	lo-lo-hi-hi
	421501	M29971	Hs.1384	O-6-methylguanine-DNA methyltransferase	lo-lo-hi-hi
	457952	U25750		Human chromosome 17q21 mRNA done 1046:1	lo-lo-hi-hi
	414630	BE410857	Hs.16064	gb:601301177F1 NIH_MGC_21 Homo saplens c	lo-lo-hi-hi
75	421990	T31811	Hs.110480	DC12 protein	lo lo hi hi
	404956			C1003210*:gii6912582 rel NP_036524.1 pe	lo lo hi hi
	436829	AW297958	Hs.163109	ESTs	lo-lo-hi-hi
	402106	AK002178		hypotherical protein FLJ11316	io-lo-hi-hi
80	404384 445123	Al762911	Hs.145369	NM_020632*Homo sapiens ATPaso, H(+)-l/a ESTs	lo-lo-hi-hi lo-lo-hi-hi
30	445123	W1/07311	116.140309	Taget Exon	lo-lo-hi-hi
	439502	AA836672	Hs.130694	ESTs	lo-lo-hi-hi
	100002				

	400111 405446	Al015709		Eos Control	lo-lo-hi-hi lo-lo-hi-hi
	401563	AJU15/U9		Homo sapiens mRNA; cDNA DKFZp58612022 (f C15001262:ci17304981 ireftNP: 038528, 11 ca	io-io-ni-ni io-io-hi-hi
	402786			C1000887*:gij12732453[refpXP_011474.1] C	lo-lo-hi-hi
5	426484	AA379658	Hs.272759	KIAA1457 protein	lo-lo-hi-hi
	414343	AL036166	Hs.323378	coated vesicle membrane protein	lo-lo-hi-hi
	421970	AF227156	Hs.110103	RNA polymerase I transcription factor RR	io-lo-hì-hì
	422592 413431	BE081857 AW246428	Hs.94211 Hs.75355	rcd1 (required for cell differentiation, ubiquitin-conjugating enzyme E2N (homolo	lo-lo-hi-hi lo-lo-hi-hi
10	426746	J03626	Hs.2057	uridine monophosphate synthetase (protat	lo-lo-hi-hi
	400237			NM_001087*:Homo sapiens ancio-associated	lo-lo-hi-hi
	402532			Target Exon	lo-lo-hì-hì
	402396 459649	AW298364	Hs.289292	Targel Exon ESTs	lo-lo-hi-hi lo-lo-hi-hi
15	401512	AVIZ98304	FIS.269292	NM_014080:Homo saplens dual oxidase-like	10-10-111-11 10-10-111-111
	448622	AL046508	Hs.270607	ESTs, Weakly similar to STK2_HUMAN SERIN	lo-lo-hi-hi
	400501			ENSP00000251912*:KIAA1617 protein (Fragm	lo-lo-hi-hi
	452324	W81486	Hs.58648	ESTs	lo-lo-hl-hi
20	453146 430445	Al338952 AW892432	Hs.32194 Hs.65307	ESTs ESTs	lo-lo-hi-hi lo-lo-hi-hi
20	401750	AW892432	HS,55307	NM_012448*:Homo sapiens signal transduce	io-lo-m-m
	435236	T03890	Hs.157208	ESTs, Highly similar to ARX MOUSE HOMEOB	lo-lo-hi-hi
	400375	NM_014115		NM_014115*:Homo saplens PRO0113 protein	lo lo hi hi
25	412151	AA100529	Hs.286232	Homo sapiens cDNA: FLJ23190 fis, clone L	lo-lo-hi-hi
23	410498	AA366749		gb:EST64459 Jurkal T-cells VI Homo saple	lo-lo-hi-hi
	405044 413169	AW161061	Hs.62954	NM_014630*:Homo saplens KIAA0211 gene pr ESTs, Weakly s'milier to zinc finger prot	lo-lo-hi-hi lo-lo-hi-hi
	402101	A1101001	110/02004	ENSP00000217725*:Laminin alpha-1 chain p	lo-lo-hi-hi
••	455019	AW850818		gb3L3-CT0220-091199-026-A03 CT0220 Homo	lo-lo-hi-hi
30	446826	AK000626	Hs.16230	hypothetical projein FLJ20619	lo-lo-hi-hi
	412180 407273	AW898791 AJ132560	Hs.118837	gb:CM0-NN0075-130400-332-406 NN0075 Homo gb:Homo sap/ens mRNA for Immunoblobulin	lo-lo-hi-hi lo-lo-hi-hi
	452895	BE389229	Hs.30954	phosphomevalonale kinase	lo-lo-H-H
	416117	H19480	Hs.268787	ESTs	lo-lo-hl-hl
35	430934	Al792302	Hs.248141	potassium inwardly-rectifying channel, s	lo-lo-hl-hl
	416309	R84694	Hs.79194	cAMP responsive element binding protein	lo-lo-hi-hi
	444578 401988	T80795	Hs.193702	ESTs C17000574:gij8923190(ref)NP_060178.1) by	lo-lo-hi-hi lo-lo-hi-hi
	444850	AW444882	Hs.148483	ESTs	(o-lo-hi-hi
40	403885	AMPHOUL	1101110	Targel Exon	lo-lo-ht-hi
	405435			Target Exon	lo-lo-hi-hi
	422694	C06003	Hs.23782	hypothetical protein FLJ12847	lo-lo-hi-hi
	422912 412748	AW405973 BE083158	Hs.11637 Hs.10862	ESTs Homo sapiens cDNA: FLJ23313 fis, clone H	lo-lo-hi-hi lo-lo-hi-hi
45	403704	BEV63130	FIS. IVOUZ	Tercel Exce	lo-lo-hì-hì
	440507	H06994		gb:y/81b07.r1 Soares Infant brain 1NIB H	lo-lo-ltl-hi
	405503			C7000609*:gij628012[pir][A53933 myosin I	lo-lo-hi-hi
	456123 454261	R00602 AF216077	Hs.48376	gbtye74c04.r1 Soares letal liver speen Homo sapiens clone HB-2 mRNA sequence	lo-lo-hì-hì lo-lo-hì-hì
50	458956	BE220675	FIS.40370	gb:hi98f11.x1 NCI_CGAP_Lu24 Homo saplens	lo-lo-hi-hi
	418367	AA326035	Hs.59236	hypothetical protein DKFZp434L0718	lo-lo-hi-hi
	444553	Al167530	Hs.149380	ESTs	lo-lo-hi-hi
	405811			NM_0248103Homo sapiens hypothelical prol	lo-lo-hi-hi
55	429461 423378	Al188219 BE313601	Hs.99311 Hs.164866	ESTs, Weekly similar to HSJ2_HUMAN DNAJ hypothetical protein FLJ22558	lo-lo-hi-hi lo-lo-hi-hi
55	458516	BE010749	Hs.255097	FSTs	lo-lo-hi-hi
	404039			ENSP00000247650":Hypollielical 177.6 kDa	lo-lo-hì-hì
	454148	AW732837	Hs.42390	nasopharyngeal carcinoma susceptibility	lo-lo-hi-hi
60	412678	AA115575	Hs.114914 Hs.171689	ESTs	lo-lo-hi-hi lo-lo-hi-hi
00	449298 405525	AI911333	MS,171689	ESTs NM_602439*tHomo saplens mutS (E. coli) h	lo-lo-hi-hi
	424576	BE154142	Hs.96833	ESTs	lo-lo-hi-hi
	451601	N92100	Hs.97437	centrosomal protein 1	lo-lo-hi-hi
65	422395	AA310177	Hs.103931	DKFZP434B0335 prolein	lo-lo-hi-hi
0.5	434333 413509	AA186733 BE145419	Hs.292154	stromal cell protein gbtl.5-HT0198-291099-009-E01 HT0198 Homo	lo-lo-hi-hi lo-lo-hi-hi
	419504	AI088585	Hs.118904	ESTs	lo-lo-hi-hi
	448586	AF285120	Hs.283734	CGI-204 emilein	lo-lo-hi-hi
	401209			C12000519:gij7710048jrefjNP_057914.1j ki	lo-lo-hi-hi
70	423554	M90516	Hs.1674	glulamine-fructose-6-phosphate transamin	lo lo hi hi
	439803 424593	AA001021 AA343729	Hs.6685	Ihyroid hormone receptor interactor 8 ab:EST49730 Gall bladder I Homo saptens	lo-lo-hi-hi lo-lo-hi-hi
	408122	Al432652	Hs.42824	hypothetical protein FLJ 10718	lo-lo-hi-hi
	409958	NM_001523	Hs.57697	hyaluronan synthase 1	lo-lo-hi-hi
75	408214	AL120445	Hs.77823	hypothetical protein FLJ21343	lo-lo-hl-hl
	421911 407813	AL041520 AL120247	Hs.40109	gb:DKFZp434G2317_s1 434 (synonym: hles3)	lo-lo-hi-hi lo-lo-hi-hi
	425211	M18667	Hs.1867	KIAA0872 protein progastriestn (pepsinogen C)	lo-lo-m-m
	442772	AW503680	Hs.5957	Homo sapiens clone 24416 mRNA sequence	lo-lo-hi-hi
80	419733	AW362955	Hs.224961	Homo sapiens cDNA FLJ14415 fis, clone HE	lo-lo-hi-hi
	428260 427083	AW290886 NM 006363	Hs.86999	ESTs, Weakly similar to S65657 alpha-1C- Sec23 (S. cerevisiae) homolog B	lo-lo-hi-hi lo-lo-hi-hi
	42/083	HW_000363	ms.173497		10-10-111-11
				1.65	

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	418583	AA604379	Hs.86211	hypothetical protein	lo-lo-hi-hi
	407355	AA846203	Hs.193974	ESTs, Weakly similar to ALU1 HUMAN ALU S	lo-lo-hì-hì
	454003	AA058944	Hs.116602	Homo saplens, clone IMAGE;4154008, mRNA,	lo-lo-hl-hi
_	425322	U63630	Hs.155637	protein kinase, DNA-activated, catalytic	lo-lo-hi-hi
5	402240			Targel Exon	lo-lo-hl-hl
	421867	AA481078	Hs.109045	hypolhetical protein FLJ10498	io-lo-hì-hì
	408603	R25283	Hs.326416	Homo sapiens mRNA; cDNA DKFZp564H1916 (f	lo-lo-hi-hi
	437389	AL359587	Hs.271586	hypolhelical protein DKFZp762M115	io-lo-hi-hi
10	457148	AF091035	Hs.184627	KIAA0118 prolein	lo-lo-hì-hì
10	400277			Eos Control	lo-lo-hì-hì
	400995			C11000295*:gi[12737279]ref[XP_012163.1]	lo-lo-hì-hì
	400818			Target Exon	io-lo-hi-hi
	402758			C1001899*:gij12722636 sefpXP_010672.1 e	lo-lo-hi-hi
1 5	403708			Targel Exon	lo-lo-hi-hi
15	405610			ENSP00000241065*:CDNA	lo-to-hi-hi
	414242	AA749230	Hs.26433	dolichyl-phosphale (UDP-N-acetylgtucosam	io-lo-hi-hi
	420757	X78592	Hs.99915	androgen receptor (dihydrotestosterone r	lo-lo-hi-hi
	400965			C11002190*:gij12737279petpXP_012163.1)	lo-lo-hi-hi
20	401192			Target Exon	lo-lo-hi-hi
20	404407			Targel Exon	lo-lo-hi-hi
	401405			Target Exon	lo-lo-hi-hi
	403055			C2002219*:gi[12737280]refpXP_006682.2[k	lo-lo-hi-hi
	404661			C9000306*gi[12737280]ref[XP_006682.2] k	lo-lo-hì-hì
25	433627	AF078866	Hs.284296	Homo saplens cDNA: FLJ22993 fls, clone K	lo-lo-hi-hi
43	410204	AJ243425	Hs.326035	early growth response 1	lo-lo-hi-hi
	432642	BE297635	Hs.3069	heal shock 70kD prolein SB (mortalin-2)	lo-lo-hi-hi
	400769			Targel Exon	lo-lo-hl-hl
	433980	AA137152	Hs.286049	phosphoserine aminolransferase	lo-lo-hi-hi
20	403725			Target Exon	lo-lo-hi-hi
30	413587	AA156164	Hs.286241	prolein kinase, cAMP-dependeni, regulato	lo-lo-hi-hi
	422614	AJ908006	Hs.295362	Homo sapiens cDNA FLJ14459 fls, clone HE	lo-lo-hì-hì
	400275			NM_006513*:Homo sapiens seryl-IRNA synth	lo-lo-hi-hi
	402810			NM_004930*:Homo sapiens capping protein	lo-lo-hi-hi
35	452049	BE268289	Hs.27693	peptidyl prolyt isomerase (cyclophilin)-i	lo-lo-hi-hi
33	445677	H96577	Hs.6838	ras homolog gene family, member E	lo-lo-hi-hi
	428770	AK001667	Hs.193128	hypothetical protein FLJ10805	lo-lo-hì-hì
	428403	AJ393048	Hs.326159	leucine rich repeat (in FLII) interactin	lo-lo-hi-hi
	434647	W74158	Hs.103189	lipopolysaccharide specific response-68	lo-to-hi-hi
40	402807			ENSP00000235229:SEMB.	lo-lo-hi-hi
40	413992	W26276	Hs.136075	RNA, U2 small nuclear	lo-lo-hi-hi
	407191	AA608751		gb:ae56h07,s1 Stratagene lung carcinoma	lo-lo-hi-lo
	403328			Target Exon	lo-lo-hi-hi
	411984	NM_005419	Hs.72988	signal Iransducer and activator of Irans	lo-lo-hi-lo
45	451017	BE391847	Hs.181173	hypothetical protein MGC10771	lo-lo-hi-hi
43	404106			C7000911*:glj4235142lgbjAAD14470.1] (AC0	lo-lo-hi-hi
	407819	R42185	Hs.102720	ESTs	lo-lo-hi-hi
	435876	AW612586	Hs.160271	G protein-coupled receptor 48	lo-lo-ti-lo
	436716 401419	Al433540		gizti69g05.x1 NCL_CGAP_Kid11 Homo sapten Taront Exon	lo-lo-hi-hi lo-lo-hi-hi
50			11- 040047		
50	424363 408866	AW512144 AW292096	Hs.346947 Hs.255036	ESTs, Weakly similar to A48809 carboxyle ESTs	lo-lo-hi-hi
		F11411	118,2000.00		lo-lo-hi-hi
	415516 423144	AW851527	Hs.253677	gb:HSC2WF081 normalized Infant brain cDN	lo-lo-hi-hi lo-lo-hi-hi
	452560	BE077084	Hs.99969	ESTs, Weakly similar to 138022 hypotheti ESTs	lo-lo-ni-ni lo-lo-hi-hi
55	439827	AA846538	Hs.187389	ESTs	
22	419709	AA255592	Hs.347973	ESTs, Weakly similar to alternatively sp	lo-lo-hi-hi lo-lo-hi-hi
	413672	BE156536	110/24/073	gb:QV0-HT0368-310100-091-h10 HT0368 Homo	lo-lo-hi-hi
	425291	AA354572		gbcEST62857 Jurkat T-cells V Homo saplen	lo-lo-hi-hi
	427403	AA402107	Hs.257146	ESTs, Moderatchy similar to 138022 hypot	lo-lo-hi-hi
60	430911	AW937461	Hs.255377	ESTs	lo-lo-hi-hi
00	435293	AI040777	Hs.117170	ESTs	lo-lo-hi-hi
	448490	Al523897	Hs.271692	ESTs, Weakly similar to 138022 hypotheti	lo-lo-hi-hi
	449539	W00363	Hs.58446	ESTs	lo-lo-hi-hi
	458082	AW978811	Hs.314451	ESTs, Weakly similar to ALU1_HUMAN ALU S	lo-lo-hi-hi
65	459407	N92114	110.014401	gbzza22h11.r1 Soares fetal liver saleen	lo-lo-hi-hi
0.5	423231	AA323486	Hs.271273	Homo sepiens cDNA FLJ12335 fis, clone MA	lo-lo-hi-hi
	450628	AW382884	Hs.204715	ESTs	lo-lo-hi-hi
	411690	AA669253	Hs.136075	RNA, U2 small nuclear	lo-lo-hi-hi
	414739	U83867	Hs.77196	spectrin, alpika, non-erythrocytic 1 (alp	lo-lo-hi-hi
70	444169	AV648170	Hs.58756	ESTs	lo-lo-hi-hi
	420911	U77413	Hs.100293	O-linked N-acetylglocosamine (GlcNAc) tr	lo-lo-hi-hi
	422195	AB007903	Hs.113082	KIAA0443 gene product	lo-lo-hi-hi
	452704	AA027823	Hs.149424	Homo saplens PNAS-130 mRNA, complete cds	lo-lo-hi-hi
	425074	AA495930	· · · · · · · · · · · · · · · · · · ·	Homo sapiens cDNA: FLJ22165 fis, clone H	lo-lo-hi-hi
75	426376	N46752	Hs.302985	ESTs	io-lo-hi-hi
	447754	AW073310	Hs.163533	Homo sapiens cDNA FLJ14142 fis. clone MA	lo-lo-hi-hi
	413686	Al469213	Hs.71404	ESTs	lo-lo-hi-hi
	449000	U69560	Hs.3826	kelch-like protein C3IP1	lo-lo-hi-hi
	430064	AK000091	Hs.231436	hypothetical protein FLJ20084	lo-lo-hi-hi
80	412205	N33818	Hs.20274	ESTs, Weakly similar to unnamed protein	lo-lo-hì-hi
	423955	Al420582	Hs.136164	culaneous T-coll lymphoma-associated turn	lo-lo-hi-hi
	455619	BE063853		gb:QV3-BT0296-011299-022-g09 BT0296 Homo	lo-lo-hi-hi

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	40872	22 AA48786	77 Hs 29810	2 ESTs	
	45971	10 AJ701596	Hs.12159		io-io-hi-hi io-io-hi-hi
	4179		5 Hs.16375		lo-lo-hi-hi
5	40296 42438		Hs.28416	NM_022095*:Homo saplens hypothetical C2H	lo-lo-hi-hi
-	42722			3 ANKHZN protein 3 RNA binding motif protein 6	(o-lo-hi-hi
	41045	51 BE06568		gb:RC3-BT0316-270400-016-f10 BT0316 Homo	lo-lo-hi-hi lo-lo-hi-hi
	40071 40721			NM 006165*:Homo saciens nuclear factor r	lo-lo-hi-hi
10	44931		3 Hs.28505 Hs.22366	Ubiquitia-conjugating enzyme F2H (homolo	lo-lo-hi-hi
	41961	2 Al498267	Hs.11061		lo-lo-hi-hi lo-lo-hi-hi
	45527	2 BE14815	2	gb:RC4-HT0231-041199-012-h04 HT0231 Home	lo-lo-hi-hi
	40183 44042		6 Hs.130760	NM_005177*:Homo sapiens ATPase, H+ Irans	lo-lo-hi-hi
15	43681				lo-lo-hi-hi lo-lo-hi-hi
	41364	4 BE15491	Hs 278790	ESTs, Weakly similar to 2195 HUMAN 21NC	lo-lo-li-hi
	41393 44819		Hs.199961	ESTs, Weakly similar to ALU7, HUMAN ALU S	lo-lo-hi-hi
	45048	8 BE62210 8 AA00999		ESTs, Weakly similar to 138600 zinc fing	lo-lo-hi-hi
20	43350	7 Al817336	Hs.191791	ESTs, Moderately similar to HPV16 E1 pro ESTs	io-lo-hi-hi lo-lo-hi-lo
	43899	6 AW74833		KIAA0421 protein	lo-lo-hi-lo
	442789 40725	9 AW90436 1 U67611	1 Hs.131191	ESTs, Weakly similar to ALU7 HUMAN ALU S	lo-lo-hi-lo
	40905	1 AA080912		Iransaldolese 1 gb:zn04d03.r1 Stratagene hNT neuron (937	lo-lo-hi-lo
25	40912	3 AA063403		gb:zm04d12.s1 Stratagene corne al stroma	lo-lo-hi-lo lo-lo-hi-lo
	41622	5 AA577730	Hs.188684	ESTs. Weakly similar to PC4259 ferritin	lo-lo-hi-lo
	433736	5 AA608955 4 AW44503		ESTs ESTs	lo-lo-hl-lo
	446667	BE161878		ESTa	lo-lo-hi-lo lo-lo-hi-lo
30	447982		Hs.137551	ESTs	lo-lo-hi-lo
	438890 427882		Hs.135049 Hs.193767	ESTs, Weakly similar to ALU7_HUMAN ALU S	lo-lo-hi-lo
	459680		Hs.42321	ESTs ESTs	lo-lo-hi-lo
25	416632	H69480	Hs.141304	ESTs	lo-lo-hi-lo lo-lo-hi-lo
35	453876 414528			ESTs, Wealtly similar to 138022 hypotheli	10-lo-h1-lo
	419902		Hs.188836 Hs.118920	ESTs ESTs	lo-lo-hi-lo
	409542	AA503020	Hs.36563	hypothetical protein FLJ22418	lo-lo-hi-lo lo-lo-hi-lo
40	433560	AJ925195	Hs.130891	hypothetical protein MGC4400	lo-lo-hi-lo
40	447499 435023	AW262580 Al892552	Hs.147674	protocadinerin beta 16	lo-lo-hi-lo
	412156	H29487	Hs.17110	gb:wd73f12.x1 NCL_CGAP_Lu24 Homo sapiens Homo sapiens mRNA; cDNA DKFZp434C2016 (f	lo-lo-hi-lo
	414505	R45389	Hs.23558	ESTs, Weakly similar to A48042 lysosomal	lo-lo-hi-lo lo-lo-hi-lo
45	404277 414662	AL036058	Hs.76807	NM_019111*:Homo sepiens major histocompa	lo-lo-hi-lo
73	444430	ALU36058 AI611153	Hs.76807 Hs.6093	mejor histocompalibility complex, class Homo saplens cDNA: FLJ22783 fis, clone K	lo-lo-hi-lo
	445612	N94128	Hs.12969	hypotherical prolein	io-io-hi-io io-io-hi-io
	403739			hypothetical protein ENSP00000251563*:UDP-glucuronosytransie	lo-lo-hi-lo
50	403740 411084	T18987	Hs.125472		lo-lo-hi-lo
	429143	AA333327	Hs.197335	ESTs, Moderately similar to KIAA0877 pro plasma glutamate carboxypeplidase	lo-lo-hi-lo o-lo-hi-lo
	443060	D78874	Hs.8944	procollagen C-endopepfidase enhancer 2	lo-lo-hi-lo
	422749 429441	W01078 AJ224172	Hs.278573 Hs.204096	CD59 antigen p18-20 (antigen Identified	lo-lo-hi-lo
55	414382	AW380339	Hs.8068	Ipophilin B (uteroglobin family member) hemalopoletic PBX-interacting protein	lo-lo-hi-lo
	441560	F13388	Hs.7888	Homo sapiens clone 23736 mRNA sequence	io-lo-hi-lo io-lo-hi-lo
	446106 452239	AA377165	Hs.44833	ESTs	lo-lo-hi-lo
	446874	AW379378 AW968304	Hs.170121 Hs.56156	protein lyrosine phosphalase, receptor t ESTs	lo-lo-hi-lo
60	412795	BE241753	Ha.74592	special AT-nich sequence hinding protein	lo-lo-hi-lo lo-lo-hi-lo
	430325 426392	AF004562 AW968324	Hs.239356	syntaxin bloding gratein 1	lo-lo-hi-lo
	420392 447448	BE244285	Hs.17384	ESTs F-box only projein 29	lo-lo-hi-lo
10	415743	AA167664	Hs.14333	ESTs, Weakly similar to Z195 HUMAN ZINC	lo-lo-hi-lo lo-lo-hi-lo
65	431607	AB033097	Hs.183669	KIAA1271 protein	lo-lo-hi-lo
	411979 453620	X85134 BE396163	Hs.25005	retinoblasioma-binding protein 5	lo-lo-hi-io
	431099	Y13367	Hs.249235	ESTs, Wealthy similar to ALU5_HUMAN ALU S phosphoirositide-3-kinase, class 2, alph	lo-lo-hi-lo
70	421687	AL035306	Hs.106823	hypolholical protein MGC14797	lo-lo-hi-lo Io-lo-hi-lo
/0	439565 442349	AF086386 W40516	Hs.145599	ESTs	lo-lo-hi-lo
	410096	AW245200	Hs.132355 Hs.267400	Homo sapiens cDNA: FLJ22119 fis, clone H	lo-lo-hi-lo
	429447	AW812452	Hs.83286	hypothetical protein MGC5540 ESTs, Wealdy similar to S14747 sphingomy	lo-lo-hi-lo lo-lo-hi-lo
75	431802	AL133570	Hs.270571	HOMO Seniore mRNA: cDMA DKEZ-4241 201 /6-	lo-lo-hi-lo
13	441715 458230	AJ929453 BE311851	Hs.342655 Hs.6639	Fromo sapiens cDNA FLJ13289 fis, clone OV	lo-lo-hi-lo
	428788	AF082283	Hs.193516	KIAA1624 protein B-cell CLL/lymphome 10	lo-lo-hi-lo lo-lo-hi-lo
	450818	AJ740573	Hs.142827	P311 protein	10-10-11-10 10-lo-hi-lo
80	419576 400401	AK002060 AF159093	Hs.91251	hypothetical protein FLJ11198	lo-lo-hi-lo
	427004	AP109093 AP921573	Hs.213107	Homo septens endogenous retrovirus RAN1 FSTe	lo-lo-hi-lo
	401178	AA046772		RNA binding molif prolein, X chromosome	lo-lo-hi-lo lo-lo-hi-lo
				167	

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	423749	U09848	Hs.132390	zinc finger protein 36 (KOX 18)	to-to-hi-lo
	428898 458258	AB033070 AW406546	Hs.194408 Hs.127971	KIAA1244 protein	io-lo-hi-lo io-lo-hi-lo
	429521	BE048708	Hs.127971 Hs.50949	ESTS	10-10-11-10 10-10-11-10
5	402185			Targel Exon	lo-lo-hi-lo
	415961	H10983	Hs.155919	ESTs	lo-lo-hi-lo
	457265 412419	AB023212 AW948630	Hs.225967	KIAA0995 protein ab: QV0-FT0001-050500-226-a05 FT0001 Homo	lo-lo-hi-lo lo-lo-hi-lo
	438397	AA806478	Hs.123206	ESTs	io-lo-hi-lo
10	440509	BE410132	Hs.134202	ESTs, Weakly similar to T17279 hypotheti	lo-lo-hi-lo
	423895 400251	AA332215		gb:EST38124 Embryo, 8 week I Homo sapien	lo-lo-hi-lo
	445094	AW296163	Hs.147296	NM_004651*:Homo sapiens ubiquitin specif ESTs	lo-lo-hi-lo
	432323	AK001409	Hs. 274356	hypothetical protein FLJ10547	lo-lo-hi-lo
15	444290	AA262496		gb;zs20f11.r1 NCI_CGAP_GCB1 Homo sapiens	lo-lo-hi-lo
	435803 436905	Z44194 N31273	Hs.4994 Hs.42380	fransducer of ERBB2, 2 ESTs	lo-lo-hi-lo lo-lo-hi-lo
	401849	14012/3	FIS.42300	Targel Exon	lo-lo-hi-lo
20	402249			C19000553*:gi[12741444[ref]XP_008888.2]	lo-lo-hi-lo
20	406180	AB018249		small inducible cylokine subternity A (Cy	lo-lo-hi-lo
	448176 409259	A)672546 AW608930	Hs.170507 Hs.52184	ESTs hypothetical protein FLJ20618	lo-lo-hi-lo lo-lo-hi-lo
	457335	AW969834	Hs.303303	ESTs	lo-lo-lti-lo
25	452444	BE144022		gb:MR0-HT0165-191199-004-105 HT0165 Homo	lo-lo-hi-lo
25	405429 430103	AA465259		Targel Exon qb:as33b03.r1 NCI_CGAP_GCB1 Homo saplens	lo-lo-hi-lo lo-lo-hi-lo
	439944	AA856767	Hs.124623	ESTs	lo-lo-hi-lo
	411283	AW852754		gb:PM1-CT0247-180100-009-c65 CT0247 Homo	lo-lo-hi-lo
30	458195	R10085	Hs.130370	ESTs	io-lo-hi-lo
30	452654 425684	BE004783 AF000989	Hs.159201	gb:MR2-BN0114-270400-004-e11 BN0114 Homo Ilhymosin, bela 4, Y chromosome	io-lo-hi-lo lo-lo-hi-lo
	429452	A)949495	Hs.133998	Homo sapiens cDNA FLJ13202 fls, clone NT	lo-lo-hi-lo
	431709	AF220185	Hs.267923	uncharacterized hypothalamus protein HTO	lo-lo-hi-lo
35	411701 430729	BE181659 AJ572560	Hs.301283	gb:QV1-HT0638-070500-191-g07 HT0638 Homo KIAA0793 gene product	lo-lo-hi-lo lo-lo-hi-lo
55	447476	BE293466	Hs.20880	ESTs, Weakly similar to 138022 hypotheti	lo-lo-ni-lo
	450438	AW293681	Hs.131887	ESTs	io-to-hi-lo
	405365			CX001212*:gij7861932 gbjAAF70445.1 (AF2 gb:nc07d11.s1 NCL_OGAP_Pr1 Homo sepiens	lo-lo-hi-lo
40	419555 448103	AA244416 U90918	Hs.13804	hypothelical protein dJ462023.2	lo-lo-hi-lo lo-lo-hi-lo
	400986			NM_024085*:Homo sapiens hypothetical pro	lo-lo-hi-lo
	424194	BE245833	Hs. 169854	gb:TCBAP1E1908 Pediatric pre-B cell acut	lo-lo-hi-lo
	400210 400234			Eos Control	lo-lo-hi-lo
45	400234			NM_005336:Homo saplens high density lipo NM_005336:Homo saplens high density lipo	lo-lo-hi-lo lo-lo-hl-lo
	405387			NM_022170*:Homo sapiens Williams-Beuren	lo-lo-hi-lo
	433075 406302	NM_002959		sortiin 1	lo-lo-hi-lo
	428181	AA423976		C16000922:gij7499103 pirjfT20903 hypothe gb:zv62h06.s1 Soares_lestls_MHT Homo sap	lo-lo-hi-lo lo-lo-hi-lo
50	456629	AW891965	Hs,279789	histone deacetylase 3	lo-lo-hi-lo
	426940	AA393537	Hs.98347	ESTs, Weakly similar to JC5308 testis-sp	lo-lo-hi-lo
	433555 421431	AA535902 AA650117	Hs.146211 Hs.283107	Homo saplens HERC2P7 pseudogene, pertial ESTs	lo-lo-hi-lo lo-lo-hi-lo
	448631	Al554923	110,200107	gb:le53h12.x1 Soeres_NFL_T_GBC_S1 Home s	lo-lo-hi-lo
55	433521	T66087	Hs.112482	Homo saplens unknown mRNA sequence	lo-lo-hi-lo
	407187 450739	AA446971 AI732707	Hs.116506	gb:zw85f11.s1 Soares_lotal_folus_Nb2HF8_	lo-lo-hi-lo lo-lo-hi-lo
	440004	BE397117	Hs.120824	ESTs, Weakly similar to ALU7_HUMAN ALU S hypothetical protein FLJ21845	lo-lo-hi-lo
	403947	NM_005032		plastin 3 (T isoform)	lo-lo-hi-lo
60	405529	AW410458		chromosome 11 open reading frame2	lo-lo-hi-lo
	402163 404663			C19001075*;gi4567179jgbjAAD23607.1jAC00 ENSP00000251684:KJAA1521 prolein (Fragme	lo-lo-hi-lo lo-lo-hi-lo
	400220			Eos Control	lo-lo-hi-lo
	401444			Target Exon	lo lo hi lo
65	455824	BE143703		gb:MR0-HT0164-191199-004-03 HT0164 Homo	lo-lo-hi-lo
	400206 458659	AW749895	Hs.332520	Eos Control Forno sapiens mRNA; cDNA DKFZp434A1014 (f	lo-lo-hi-lo lo-lo-hi-lo
	428666	AL080190	Hs.189242	Homo sapiens mRNA; cONA DKFZp434A202 (fr	lo-lo-hi-lo
70	428442	AA428638	Hs.98606	ESTs	lo-lo-ht-lo
70	440151 431046	AA868167 AW854382	Hs.249126	gb:sk38a07.s1 Soares_lestis_NHT Homo sap Homo sapiens clone 24894 mRNA sequence	lo-lo-hi-lo lo-lo-hi-lo
	443914	A/091173	Hs.222362	ESTs, Weakly similar to p40 [H.sapiens]	lo-lo-hi-lo
	402469			Target Exon	lo-lo-hi-lo
75	418155 446893	R45481 41610818	Hs.23719 Hs.7110	ESTs, Weakly similar to 138022 hypotheti	lo-lo-hi-lo lo-lo-hi-lo
13	446893	AW340958	Hs.7572	ESTs ESTs	lo-lo-hi-lo
	421290	NM_014368	Hs.103137	LIM homeobox protein 6	lo-lo-hi-lo
	450374	AA397540	Hs.60293	Homo sapiens clone 122482 unknown mRNA	lo-lo-hi-lo
80	402347 415184	AA380436	Hs.211973	Targel Exon homolog of Yeasl RRP4 (ribosomal RNA pro	lo-lo-hi-lo lo-lo-hi-lo
	415632	U67085	Hs.78524	TcD37 homolog	lo-lo-hi-lo
	423718	AL119520	Hs.180737	Homo sapiens clone 23664 and 23905 mRNA	lo-lo-hi-lo

	449140	AW013840	Hs.202092	ESTs	lo-lo-hi-lo
	431241	AA496799	Hs.36958	ESTs	lo-lo-hi-lo
	416631	H69466		gb:yr88f07.r1 Soares fetal liver spleen	lo-lo-hi-lo
5	424168 401600	L29277 BE247275	Hs.321677	signal transducer and activator of trans	lo-lo-hi-lo lo-lo-hi-lo
,	420588	AF000982	Hs.147916	US snRNP-specific protein, 116 kD DEAD/H (Asp-Glu-Ala-Asp/His) box polypep	lo-lo-hi-lo
	414111	BE047679	Hs.152982	hypothetical protein FLJ13117	lo-lo-hi-lo
	417138	AA193646	Hs.65771	Homo sapiens chromosome 19, BAC CIT-HSPC	lo-lo-hi-lo
	424318	AA476515	Hs.172723	ESTs	lo-lo-hi-lo
10	455653	BE154075		gb:PM0-HT0339-200400-010-E05 HT0339 Homo	lo-lo-hi-lo
	451493	H38656	Hs.32854	ESTs	lo-lo-hi-lo
	457015	AA688058	Hs.261544	ESTs	lo-lo-hi-lo
	403654			NM_003071:Homo sapiens SWI/SNF related, FSTs	lo-lo-hi-lo
15	435203 409322	AW957127 BE091159	Hs.294027 Hs.22687	ESTs, Moderately similar to unnamed prot	lo-lo-hi-lo lo-lo-hi-lo
13	437764	AA767795	Hs,166832	ESTs	lo-lo-hi-lo
	432542	AW083920	Hs.16098	claudin 2	lo-lo-hi-lo
	436125	AA765895	Hs.152895	ESTs	lo-lo-ht-lo
	403217	AL134878		ribosomal protein, large P2	lo-lo-ini-lo
20	434023	Al277883	Hs.146141	ESTs	lo-lo-hi-lo
	442419	AI749893	Hs.270532	ESTs, Weakly similar to I38022 hypotheti	lo-lo-hi-lo
	443667	Al129066	Hs.135457	ESTs	lo-lo-hi-lo
	451445	AA017609 BE160229	Hs.343449	gb:ze37e01.r1 Soares retina N2b4HR Homo gb:QV1-HT0413-090200-062-e12 HT0413 Homo	lo-lo-hi-lo lo-lo-hi-lo
25	454775 411053	AW615061		gb:CMO-ST0209-271099-082-d10 ST0209 Homo	lo-lo-hi-lo
23	435312	AJ243396	Hs.4865	vcitage-galed sodium chennel beta-3 subu	lo-lo-hi-lo
	450875	AK000724	Hs.301553	karyopherin alpha 6 (importin alpha 7)	lo-lo-hi-lo
	451180	H61899	Hs.171937	steroid dehydrogenase-like	lo-lo-hi-lo
	427327	AW501456	Hs.288283	Homo saplens cDNA: FLJ22355 fls, clone H	lo-lo-hi-lo
30	444321	AW204210	Hs.122275	Homo sapiens mRNA; cDNA DKFZp564N1623 (f	lo-lo-hi-lo
	405109	N47812		CGI-35 protein	lo-lo-hi-lo
	450182	Al796400	Hs.240767	Human DNA sequence from clone RP1-12G14	lo-lo-hi-lo lo-lo-hi-lo
	424990 428997	AU076896 AF085391	Hs.154095 Hs.194718	zinc finger protein 143 (clone pHZ-1) zinc finger protein 265	10-10-11-10 10-10-11-10
35	402602	AF065391	HS.194716	NM_021186*:Homo sapiens zona pellucida g	lo-lo-hi-lo
55	426772	AJ524039	Hs.192524	ESTs	lo-lo-hi-lo
	423759	Al142358	Hs.184361	ESTs, Moderately similar to ALU7_HUMAN A	lo-lo-hi-lo
	434350	AL042940	Hs.93872	KIAA 1682 protein	lo-lo-hi-lo
	442274	Al733484	Hs.129182	ESTs	lo-lo-hi-lo
40	442884	AJ076570	Hs.134053	ESTs	lo-lo-lnl-lo
	400481			Target Exon	lo-lo-hi-lo
	407283	T51008		gb:yb55e08.s1 Stratagene ovary (937217)	lo-lo-hi-lo
	408859 455615	AW291672 BE045344	Hs.258981 Hs.274923	ESTs Moderately similar to unnamed prot	lo-lo-hi-lo lo-lo-hi-lo
45	427315	AA179949	Hs.175563	Homo sapiene mRNA; cDNA DKFZp564N0763 (f	lo-lo-hi-lo
75	449375	R07114	Hs.271224	ESTs	lo-lo-hi-lo
	419937	AB040959	Hs.93836	DKFZP434N014 protein	lo-lo-hi-lo
	422231	AA443512	Hs.101383	ESTs	lo-lo-hi-lo
70	437210	AA311443	Hs.293563	Homo sapiens mRNA; cDNA DKFZp588E2317 (f	lo-lo-hi-lo
50	418056	AA524886		gb:nh34f02.s1 NCI_CGAP_Pr3 Homo sapiens	lo-lo-hi-lo
	448588 407949	N58790 W21874	Hs.268820 Hs.247057	ESTs	lo-lo-hi-lo lo-lo-hi-lo
	440296	D30629	Hs.180610	ESTs, Weakly similar to 2109/260A B cell splicing factor proline/glutamine rich (lo-lo-hi-lo
	422280	AA315993	Hs.105484	regenerating gene type IV	lo-lo-hi-lo
55	434685	AA642445	H\$.287467	Homo sapiens cDNA FLJ11948 fis, clone HE	lo-lo-hi-lo
50	412657	AW976165	1141201141	gb:EST388274 MAGE resequences, MAGN Homo	lo-lo-hi-lo
	405188			Target Exon	lo-lo-hHo
	416954	AJ222358		gb:qh04c12.x1 Soares_NFL_T_GBC_S1 Homo s	lo-lo-hi-lo
60	423700	AA232375	Hs.58606	SNRPN upstream reeding frame	lo-lo-hi-lo
00	430288	BE394943	Hs.13804 Hs.135127	hypothetical protein dJ462023.2 ESTs, Weakly similar to unnamed protein	lo-lo-hi-lo lo-lo-hi-lo
	435184 431475	T67162 Al567669	Hs.40342	putative nuclear protein	lo-lo-hi-lo
	445239	Al217375	Hs.170023	ESTs, Weakly similar to CA36_HUMAN COLLA	lo-lo-hi-lo
	436151	AK000801	Hs.324271	Homo sapiens cDNA FLJ20794 fis, clone CO	lo-lo-hi-lo
65	448489	Al523875		gb:tg97d04.x1 NCI_CGAP_CLL1 Homo sapiens	lo-lo-hi-lo
	424470	BE244261	Hs.323502	Homo sapiens cDNA: FLJ23539 fis, clone L	lo-lo-hi-lo
	434733	Al334367	Hs.159337	ESTs	lo-lo-hi-lo
	409469	AW517236	Hs.335762	ESTs	lo-lo-hi-lo
70	414034	U89277	Hs.305985	early development regulator 1 (homolog o	lo-lo-hi-lo lo-lo-hi-lo
/0	420382 430433	AW959165 AA478883	Hs.270034 Hs.273766	Homo sapiens, Similar to nuclear localiz ESTs	10-10-11-10 10-10-11-10
	435351	T80177	Hs.118064	similar lo rat nuclear ubiquitous casein	lo-lo-hi-lo
	403218	AL134878		ribosomal protein, large P2	lo-lo-hi-lo
	420678	AW593288	Hs.3530	TLS-associated serine-arginine protein 2	lo-lo-hi-lo
75	445808	AV655234		ESTs, Moderately similar to PC4259 ferri	lo-lo-hi-lo
	429933	AA765596	Hs.187691	ESTs	lo-lo-hi-lo
	419802	AA250950	Hs.154334	ESTs	lo-lo-hi-lo
	425155	W26522	Hs.75890	gb:32g2 Human retina cDNA randomly prime gb:za11c01.s1 Soares fetal liver spleen	lo-lo-hi-lo lo-lo-hi-lo
80	417314 428290	N68168 AI932995	Hs.183475	go:zanteun.st soares tetal (ver spicen Homo sapiens clone 25061 mRNA sequence	lo-lo-hi-lo
30	420290	AW681145	· a.1004/0	gb:QV0-OT0033-010400-182-a07 OT0033 Homo	lo-lo-ti-lo
	432014	H66741	Hs.38540	ESTs, Weskly similar to ALU4_HUMAN ALU S	lo-lo-hi-lo

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	407351	AW383165		gb:PM3-HT0344-151299-004-107 HT0344 Homo	lo-io-hi-lo
	443231 444001	W87548 Al095087	Hs.132932 Hs.152299	ESTs ESTs, Moderalely similar to S65657 alpha	lo-lo-hi-lo lo-lo-hi-lo
	435064	T70740	Hs.31433	ESTs	lo-lo-hi-lo
5	435173	AW295645	Hs.255451	ESTs	lo-lo-hi-lo
	411831	AW994394		gb:RC3-BN0036-060400-014-h12 BN0036 Homo	lo-lo-hi-lo
	446572 428114	AV659151 AI821548	Hs.282961 Hs.98363	ESTs ESTs, Weakly s'milar to 138022 hypotheti	lo-lo-hi-lo lo-lo-hi-lo
	406207	A1021040	118.30000	Target Exon	lo-lo-hi-lo
10	405011			Target Exon	lo-lo-hi-lo
	409451 411233	AF012626 AW833793	Hs.54472	fragile X mental retardation 2 gb:QV4-TT0008-130100-080-a06 TT0008 Homo	lo-lo-hi-lo lo-lo-hi-lo
	455729	BE072092		gb:PM4-BT0532-160200-003-b11 BT0532 Homo	10-10-11-10 10-10-hi-10
	439454	AA836120	Hs.258958	ESTs	lo-lo-hi-lo
15	445124	AI806403	Hs.143942	ESTs	lo-lo-hi-lo
	410324 446548	AW292539 AJ769392	Hs.30177 Hs.200215	ESTs ESTs	lo-io-hi-lo Io-lo-hi-lo
	416999	AW195747	Hs.21122	hypothetical prolein FLJ11830 similar to	lo-lo-hi-lo
	414553	AJ813865	Hs.164478	hypothetical protein FLJ21939 similar to	lo-lo-hi-lo
20	444647	H14718	Hs.11506	Human clone 23589 mRNA sequence	lo-lo-hi-lo
	418271 407939	NM_000919 W05608	Hs.83920 Hs.312679	peptidylglycine alpha-amidaling monocxyg ESTs, Wealdy similar to A49019 dynein he	lo-lo-hi-lo lo-lo-hi-lo
	432676	AI187366	116.012013	gb:qf29c01.x1 Soares_testis_NHT Homo sap	lo-lo-hi-lo
~ ~	415156	X84908	He.78060	phosphorylase kinase, beta	lo-lo-hi-lo
25	432679	Al146956	Ha.146723	ESTs, Weakly similar to A53950 transcrip-	10-lo-hi-lo
	412121 418858	AB033061 AW961605	Hs.73287 Hs.21145	KIAA1235 protein hypothetical protein RG083M05.2	lo-lo-hi-lo lo-lo-hi-lo
	425204	NM 002436		membrane protein, palmiloylated 1 (55kD)	lo-lo-hi-lo
••	418348	Al537167	Hs.96322	hypothetical prolein FLJ23560	lo-lo-hi-lo
30	410765	A)694972	Hs.66180	nucleosome assembly protein 1-like 2	lo-lo-hi-lo
	445594 416503	AW058463 H98502	Hs.12940 Hs.269853	zinc-fingers and homeoboxes 1 ESTs	lo-lo-hi-lo lo-lo-hi-lo
	426167	AF039023	Hs.167496	RAN binding protein 6	lo-lo-hi-lo
25	451752	AB032997	Hs.26966	KIAA1171 protein	lo-lo-hi-lo
35	447124 419872	AW976438 A/422951	Hs.17428 Hs.146162	RBP1-like protein ESTs	lo-lo-hi-lo lo-lo-hi-lo
	443161	A/038316	ns.140102	gb:tox48c08.x1 Soares_total_fetus_Nb2HF8_	lo-lo-hi-lo
	445391	T92576	Hs.191168	ESTs	lo-lo-hi-lo
40	443801	AW206942	Hs.253594	intron of: trichorhinophalangeal syndro	lo lo hi lo
40	448708 428172	AW807831 U09367	Hs.190488 Hs.182828	Homo sapiens, Similar to nuclear localiz zinc finger protein 136 (clone pHZ-20)	lo-lo-hi-lo lo-lo-hi-lo
	421021	AA808018	Hs.109302	ESTs	lo-lo-hi-lo
	431749	AL049263	Hs.306292	Homo saplens mRNA; cDNA DKFZp564F133 (fr	ko-lo-hi-ko
45	423784	AK000039	Hs.132826	Homo sepiens cDNA FLJ14913 lis, clone PL	lo-lo-hi-lo
43	419479 450900	AJ288348 H61005	Hs.23450 Hs.37902	mitochondrial ribosomal protein S25 ESTs	lo-lo-hi-lo lo-lo-hi-lo
	423396	Al382555	Hs.127950	bromodomain-containing 1	lo-lo-hi-lo
	426137	AL040683	Hs.167031	DKF2P566D133 protein	lo-lo-hi-lo
50	442012	AI733277	Hs.128321	ESTs FSTs	lo-lo-hi-lo
50	452271 414882	AA025976 D79994	Hs.34569 Hs.77546	Homo saplens cDNA: FLJ21983 fis, clone H	lo-lo-hi-lo lo-lo-hi-lo
	432195	AJ243669	Hs.8127	KIAA8144 gene product	io-lo-hi-lo
	430217	N47863	Hs.180450	ribosomal protein S24	io-lo-hi-io
55	429567 438810	R35606 AW897846	Hs.326800 Hs.6421	Human EST clone 53125 mariner transposon hypothetical protein DKFZp761N09121	lo-lo-hi-lo lo-lo-hi-lo
55	436796	BE515260	Hs.5320	hypothetical protein	ko-lo-hi-ko
	428352	N72324	Hs.55098	ESTs	lo-lo-hi-lo
	415308	F05251	11 0-0-4	gb:HSC04H101 normalized infant brain cDN	lo-lo-hì-lo
60	420148 434442	U34227 AA737415	Hs.95361 Hs.152828	myoeln VIA (Usher syndrome 1B (autosoma ESTs	lo-lo-hi-lo lo-lo-hi-lo
00	449429	AA054224	Hs.59847	ESTs	lo-lo-hi-lo
	410245	C17908	Hs.194125	ESTs	lo-lo-hi-lo
	421168 436237	AF182277 R11528	Hs.330780 Hs.271968	cytochrome P450, subfamily IIB (phenober ESTs.	io-lo-hi-lo Io-lo-hi-lo
65	440668	AI989538	Hs.191074	ESTs	lo-lo-hi-lo
00	422068	AI807519	Hs.104520	Homo saplens cDNA FLJ13694 fis, clone PL	lo-lo-hi-lo
	410216	BE061839		gb:RC1-BT0254-290100-015-a05 BT0254 Homo	lo-lo-hi-lo
	439437 417061	AJ207788 AJ675944	Hs.343628 Hs.188691	sialyttransferase 4B (beta-galactosidase Homo sapiens cDNA FLJ12033 fis, clone HE	lo-lo-hi-lo lo-lo-hi-lo
70	403046	M2010344	Ha-1000a1	NM_005656":Homo sapiens transmembrane pr	lo-lo-til-lo
	404528	AI912555		peptide YY, 2 (seminalplesmin)	lo-lo-hi-lo
	439734	AC005013	Hs. 149	cAMP response element-binding protein CR	lo-lo-hi-lo
	452997 403745	N64777	Hs.44656	ESTs ENSP00000226812*:KIAA1494 protein (Fragm	lo-lo-hi-lo lo-lo-hi-lo
75	411448	AA178955	Hs.271439	ESTs, Weakly similar to 138022 hypotheti	lo-lo-hi-lo
	422460	AW445014	Hs.197746	ESTs	ko-ko-hii-lo
	404058 436184	BE154067	Hs.136660	Target Exon ESTs, Weakly similar to ZN91, HUMAN ZINC	lo-lo-hi-lo lo-lo-hi-lo
	436184 427702	BE154067 N76589	Hs.139960 Hs.14454	ESTs, Weakly similar to ZN91_HUMAN ZINC ESTs, Weakly similar to TFIID subunit TA	lo-lo-hi-lo
80	440695	AW088363	Hs.246240	ESTs	lo-lo-hi-lo
	424881	AL119690	Hs.153618	HCGVIII-1 protein	lo-lo-hi-hi
	440573	BE550891	Hs.270624	ESTs	lo-lo-hi-hi

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	416659 436731	W22048 AA580691	Hs.64753 Hs.180789	glu61A12 Human relina dDNA Tsp6094-clcav S164 protein	lo-lo-hi-l lo-lo-hi-l
	405102			C15001220*:gij4469558lgbjAAD21311.1] (AF	lo-lo-hi-i
5	450219 404527	AI826999 AI912555	Hs.224624	ESTs peptide YY, 2 (seminalplasmin)	lo-lo-hi-l lo-lo-hi-l
-	439158	R60323	Hs.193888	ESTs	lo-lo-hi-l
	431952	Z70695	Hs.272240	Homo sapiens cDNA FLJ11086 fis, clone PL	lo-lo-hi-i
	418584 424241	NM_004606 AW995948	Hs.1179 Hs.182339	TATA box binding protein (TBP)-associate	lo-lo-hi-l lo-lo-hi-l
10	410124	AW962229	Hs.128927	Homo sapiens pyruvate deliydrogenase kina Homo sapiens cDNA FLJ13903 fis, clone TH	lo-lo-ni-r
	435955	AA830515	Hs.222917	ESTs	lo-lo-hi-t
	424001	W67883 A/630844	Ha.137476	paternally expressed 10	hi-hi-lo-l
	441399 440184	A/630844 AB002297	Hs.126919 Hs.7022	ESTs dedicator of cyto-kinesis 3	hi-hi-lo-l hi-hi-lo-l
15	421996	AW583807	Hs.1460	glucagon	hi-hi-lo-l
	444252	R21135	Hs.54985	ESTs	hi-hi-lo-l
	402082			C18000743*:gij6678363jref[NP_033416.1] i	hi-hi-lo-i
	405396 412457	T32587	Hs.170414	C22000452*:gij6961522jreljNP_036781.1j r paired basic amino acid cleaving system	hi-hi-lo-l hi-hi-lo-l
20	415808	R21439	Hs.334578	Homo sapiens, clone IMAGE:3929520, mRNA	hi-hi-lo-l
	441494	AW452344	Hs.129977	ESTs	hi-hi-lo-l
	437330	AL353944	Hs.50115	Homo sapiens mRNA; cDNA DKFZp761J1112 (f	hi-hi-lo-l
	452784 410037	BE463857 AB020725	Hs.151258 Hs.58009	hypothetical protein FLJ21062	hi-hi-lo-l hi-hi-lo-l
25	449145	A)632122	Hs.198408	KIAA0918 protein ESTs	hi-hi-lo-i
	452487	AW207659	Hs.6630	Homo sapiens cDNA FLJ13329 fis, clone OV	hi-hi-lo-l
	431031	AA830335	Hs.105273	ESTs	hi-hi-lo-l
	427209 434280	H06509 BE005398	Hs.92423	KIAA1566 protein qb:CM1-BN0116-150400-189-h02 BN0116 Homo	hi-hi-lo-l
30	418236	AW994005	Hs.337534	ESTs	hi-hi-lo-l
-	429201	X03178	Hs.198246	group-specific component (vitamin D bind	hi-N-lo-l
	416653	AA768553	Hs.193145	metallothlonein 1E (functional)	hi-hi-lo-l
	422501	AA354690 R62424	Hs.144967	ESTs	hi-hi-lo-l
35	425087 426798	AA385062	Hs.126059 Hs.130260	ESTs ESTs	hi-hi-lo-l
	443798	R07848	Hs.188522	ESTs	hi-hi-lo-l
	427254	AL121523	Hs.97774	ESTs	H-H-10-1
	431657 409963	Al345227 AA133590	Hs.105448 Hs.250857	ESTs, Weakly similar to B34087 hypotheti cafcium/caimodulin-dependent protein kin	hi-hi-lo-l hi-hi-lo-l
40	446006	NM_004403		deafness, autosomal dominant 5	hi-hi-to-t
	418259	AA215404	110.10000	ESTs	hi-hi-lo-l
	410173	AA706017	Hs.119944	ESTs	hi-hi-lo-k
	436023 448428	T81819 AF282874	Hs.302251 Hs.21201	ESTs nectin 3; DKFZP566B0846 protein	hi-hi-lo-li hi-hi-lo-li
45	430665	BE350122	Hs.157367	ESTs, Weakly similar to 178885 serine/th	hi-hi-lo-k
	432559	AW452948	Hs.257631	ESTs	hi-hi-lo-k
	451572	AA018556	Hs.268691	ESTs, Moderetely similar to ALU2_HUMAN A	hì hi lo l
	458032 438209	AW957446 AL120659	Hs.301711 Hs.6111	ESTs aryl-hydrocarbon receptor nuclear transl	hi-hi-ko-k hi-hi-ko-k
50	438337	AK002058	Hs.6166	hypothetical protein FLJ11196	hi-hi-lo-k
	431795	AK002088	Hs.270124	Homo saplens cDNA FLJ11226 fis, clone PL	hi-hi-lo-k
	421114	AW975051 AA516420	Hs.293156	ESTs, Weakly similar to 178885 serine/th	hi-hi-lo-i hi-hi-lo-k
	431843 440948	AA516420 AW188311	Hs.128619	ESTs, Weskly similar to 138022 hypotheti ESTs	m-ni-to-te
55	430105	X70297	Hs.2540	cholinergic receptor, nicotinic, alphe p	hi-hi-lo-li
	439046	AA947354		gb:od86e11.s1 NCI_CGAP_Ov2 Homo sapiens	hi-hi-lo-k
	451491	Al972094	Hs.286221	Homo saplens cDNA FLJ13741 fis, clone PL	hi-hi-lo-k hi-hi-lo-k
	452789 419829	AW081626 Al924228	Hs.242561 Hs.115185	ESTs Moderately similar to PC4259 femi	hi-hi-lo-k
60	449567	A1990790	Hs.188614	ESTs	hi-hi-lo-l
	407787	N21307	Hs.13477	ESTs, Weakly similer to 1207289A reverse	hi-hi-lo-k
	409091	AW970388	Hs.269423	ESTs	hi-hi-io-k hi-hi-io-k
	435354 444809	AA678267 BE207568	Hs.117115 Hs.208219	ESTs oculospanin	m-m-ro-ro
65	422170	Al791949	Hs.112432	anti-Mullerian hormone	hi-hi-lo-k
	453582	AW854339	Hs.33476	hypothetical protein FLJ11937	hihidok
	435905	AW997484	Hs.5003	KIAA0456 protein	hi-hi-lo-k
	443884 430027	N20617 AB023197	Hs,194397 Hs,227743	leptin receptor KIAA0980 protein	hi-hi-lo-k hi-hi-lo-k
70	432582	A)623817	Hs.168457	ESTs	hi-hi-lo-k
	417993	AW963705	Hs.301183	molecule possessing ankyrin repeats Indu	hi-hi-lo-k
	444930	BE185536	Hs.301183	molecule possessing ankyrin repeats indu	hi-hi-lo-i
	427794 410913	AA709186 AL050367	Hs.99070 Hs.66762	ESTs Homo sapiens mRNA; cDNA DKFZp564A026 (fr	hi-hi-lo-k hi-hi-lo-k
75	431992	NM_002742	Hs.2891	protein kinase C, mu	hi hi lo k
	447846	AA324057	Hs.77955	Homo sapiens cDNA: FLJ23527 fis, clone L	hi-hi-lo-k
	430439 432621	AL133561 Al298501	Hs.12807	DKF2P434B061 protein ESTs, Wealdy similar to T46428 hypotheti	hi-hi-lo-k hi-hi-lo-k
	432621	AK000401	Hs,252748	ES1s, Weakly similar to 146428 hypotheti Homo sapiens cDNA FLJ20394 fis, close KA	hi-hi-lo-k
80	408872	A/478139	Hs.13291	ESTs	ti-hi-lo-k
	453200	AA033832	Hs.212433	ESTs	hi-hi-lo-le
	411529	AA430348	Hs.317596	Homo sapiens cDNA FLJ12927 fis, clone NT	hi-hi-lo-li
				171	

	414483	R25513	Hs.10683	ESTs	hi-hi-lo-lo
	451273	NM_014811		KIAA0649 gene product	hi-hi-lo-lo
	437052 440049	AA861697	Hs.120591	ESTs	hi-hi-lo-lo
5	429483	R06699 AA974832	Hs.19769 Hs.128708	hypothetical protein MGC4174 ESTs	hi-hi-lo-lo hi-hi-lo-lo
,	411296	BE207307	Hs.10114	growth suppressor 1	hi-hi-lo-lo
	425188	AK002052	Hs.155071	hypothetical protein FLJ11190	hi-hi-lo-lo
	436315	BE390513	Hs.27935	hypothetical prolein MGC4837	hi-hi-lo-lo
	400297	Al127076	Hs.306201	hypothetical protein DKFZp564O1278	hi-hi-lo-lo
10	431089	BE041396		ESTs, Weakly similar to unknown protein	hi-hi-lo-lo
	418824	AW751661	Hs.53542	choreoacanthocytosis gene; KIAA0986 prot	hi-hi-to-lo
	449226	AB002366	He 23311	KIAA0367 protein	hi-hi-lo-lo
	450149	AW969781	Hs.132863	Zic family member 2 (odd-paired Drosophi	hi-hi-lo-lo
1.5	418443	NM_005239		v-els avian erythroblastosis virus E26 o	hi-hi-lo-lo
15	458692	BE549905	Hs.231754	ESTs	hi-hi-lo-lo
	410102	AW248508	Hs.279727	ESTs; homologue of PEM-3 [Clons savignyl	hi-hi-lo-io
	451062 407633	AL110125 NM 007069	Hs.25910 Hs.37189	Homo saplens mRNA; cDNA DKFZp564C1416 (f similar to ral HREV107	hi-hi-lo-lo hi-hi-lo-lo
	418941	AA452970	Hs.239527	E1B-55kDe-associated protein 5	hi-hi-lo-lo
20	407059	X95406	H5.20802/	gb:H.sapiens cyclin E gene.	hi-hi-lo-lo
20	455956	BE162704		gb:PM1-HT0454-301299-001-d08 HT0454 Homo	hi-hi-lo-lo
	437763	AA469369	Hs.5831	tissue inhibitor of metalloproteinase 1	hi-hi-lo-lo
	451404	AA460775	Hs.6295	ESTs, Weekly similar to T17248 hypotheti	hi-hi-lo-lo
	428494	AA233439	Hs.184634	hypothetical protein FLJ20005	hi-hi-lo-lo
25	414957	D61283	Hs.45206	ESTs	hi-hi-lo-io
	456415	Al734051	Hs.277102	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-hi-lo-lo
	400183			Eos Control	hi-hi-lo-lo
	400158			ENSP00000244302*:CDNA FLJ11591 fils, clon	hi-hi-io-lo
20	403893			ENSP00000237068*:Protocadherin alpha 6 p	hi-hi-lo-lo
30	423809	Al223833	Hs.154483	ESTs	hi-hi-lo-lo
	400170			Eos Control	hi-hi-lo-lo
	403291 422026		Hs.110826	Targel Exon	hi-hi-lo-lo hi-hi-lo-lo
	417130	U80736	Hs.81256	trinscleotide repeal containing 9	ni-ni-lo-lo hi-hi-lo-lo
35	432472	AW276858 AA548781	Hs.81255 Hs.136418	S100 calcium-blinding protein A4 (calcium ESTs	hi-hi-lo-lo
55	405231	AND40101	HS.130416	C2001066xpl10257425(ref NP_033892.1) CD	hi-hi-lo-io
	400141			Eos Control	hi-hi-lo-to
	428971	BE278404	Hs.285813	hypothetical protein FLJ11807	hi-hi-io-lo
	422390	AW450893	Hs.121830	ESTs, Weekly similar to T42682 hypotheti	hi-hi-lo-lo
40	425538	BE270918	Hs.184026	Homo saplens, clone IMAGE:3534875, mRNA,	hi-hi-lo-lo
	456972	AJ054347	Hs.2017	ribosomal protein L38	hi hi lo lo
	456622	AF205849	Hs.107740	Kruppel-like factor 2 (lung)	hi-hi-lo-lo
	418515	AJ568453	Hs.19487	ESTs, Weakly similar to CNIH_HUMAN CORNI	hi-hi-lo-lo
4.5	448439	BE613082	Hs.28229	ARG99 protein	hi-hi-lo-lo
45	445418	AW139377	Hs.127179	cryplic gene	hi-hi-io-io
	402559	Z23024		Rho GT Pase activating protein 1	hi-hi-io-io
	402675	Z23024		Rho GTPase activating protein 1	hi-hi-lo-lo
	420811 446627	AA807544 A8973016	Hs.15725	ESTs, Weakly similar to B34323 GTP-bindi hypothetical protein SBB48	hi-hi-lo-lo hi-hi-lo-lo
50	400247	METOUTO	115.10120	Eos Control	hi-hi-io-io
50	430289	AK001952	Hs.238039	hypothetical protein FLJ11090	hi-hi-lo-lo
	400133	741001002	HALLOGOOD	Eos Control	hl-hì-lo-lo
	418816	T29621	Hs.88778	carbonyl reductase 1	hi-hi-lo-lo
	433579	BE264473	Hs,284297	hypothetical protein from EUROIMAGE 1967	hi-hi-lo-lo
55	401952			Target Exon	hi-hi-lo-lo
	410349	AW663021	Hs,323445	ESTs, Weakly similar to T2D3_HUMAN TRANS	hi-hi-lo-lo
	417558	AF045229	Hs.82280	regulator of G-protein signalling 10	hì-hi-lo-lo
	446851	AW007332	Hs.10450	Homo sapiens cDNA: FLJ22063 fis, clone H	hi-hi-lo-lo
60	404489			Target Exon	hi-hi-lo-lo
60	405802			Target Exon	hi-hi-lo-lo
	456266	L29073	Hs.198726	cold shock domain protein A	hi-hi-lo-lo
	457133 459330	M54968		v-Ki-ras2 Kirsten ral sarcoma 2 viral on	hi-hi-lo-lo hi-hi-lo-lo
	433041	C16931 BE265848	Hs.289080	gb:C16931 Clontech human aorta polyA mRN colon cancer-associated protein Mic1	lo-lo-lo-hi
65	446545	Al431798	Hs.164192	ESTs, Weakly similar to Y161_HUMAN HYPOT	lo-lo-lo-l\(\)
00	414911	NM 000107	Hs.77602	damage-spectic DNA binding protein 2 (4	lo-lo-lo-hi
	414682	AL021154	Hs.76884	inhibitor of DNA binding 3, dominant neg	lo-lo-lo-hi
	422311	AF073515	Hs.114948	cylokine receptor-like factor 1	lo-lo-lo-hi
	447329	BE090517		ESTs, Moderately similar to ALUS_HUMAN A	lo-lo-lo-hi
70	412942	AL120344	Hs.75074	mitogen-activated protein kinase actival	lo-lo-lo-hi
	420747	BE294407	Hs.99910	phosphofruciokinase, platelel	lo-lo-lo-hi
	431912	A)660552	Hs.76549	ESTs, Weakly similar to A56154 Abi subst	lo-lo-lo-hi
	446506	Al123118	Hs.15159	chemokine-like factor, alternatively spl	lo-lo-lo-hi
75	408633	AW963372	Hs.46677	PRO2000 protein	lo-lo-lo-hi
/5	433675	AW977653	Hs.75319	ribonucleolide reductase M2 polypeptide	hi-lo-lo-hi
	424560	AA158727 AW152225	Hs.150555 Hs.165909	protein predicted by clone 23733	hi-lo-lo-hi hi-lo-lo-hi
	425234			ESTs, Weekly similar to 138022 hypotheli	
	439815 410174	AA206079 AA306007	Hs.6693 Hs.59461	hypothetical protein FLJ20420 DKFZP434C245 protein	hi-lo-lo-hi hi-lo-lo-hi
80	410442	X73424	Hs.63788	propionyl Coenzyme A carboxylase, beta p	hi-lo-lo-hi
	429190	H18650	Hs.92602	FSTe	hi-lo-lo-hi
	423619	T48691	Hs.249159	adrenergic, alpha-2A-, receptor	hi-lo-lo-hi
				172	

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	433764	AW753676	Hs.39982	ESTs	hi-lo-lo-hi
	421998	R74441	Hs.117176	poly(A)-binding protein, nuclear 1	hi-lo-lo-hi
	451593 452092	AF151879 BE245374	Hs.26706 Hs.27842	CGI-121 protein hypothelical protein FLJ11210	hi-lo-lo-hi hi-lo-lo-hi
5	447425	Al963747	Ha.18573	acylphosphatase 1, erythrocyte (common)	hi-lo-lo-hi
	421654	AW163267	Hs.106469	suppressor of var1 (S.corevisiae) 3-like	hi-lo-lo-hi
	432502 429597	NM_014641 NM 003816	Hs.277585 Hs.2442	KIAA0170 gene product a distintegrin and metallogroteinase doma	hi-lo-lo-hi hi-lo-lo-hi
	434203	BE262677	Hs.2442 Hs.283558	a dismegrin and metalloproteinase doma hypothetical protein PRO1855	ni-lo-lo-ni hi-lo-lo-ni
10	438461	AW075485	Hs.286049	phosphoserine aminotransferase	hi-lo-lo-hi
	409142	AL135877	Hs.50758	SMC4 (structural maintenance of chromoso	hi-lo-lo-hi
	439574 438182	AJ469788 AW342140	Hs.165190 Hs.182545	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-lo-lo-hi hi-lo-lo-hi
	449103	T24968	Hs.23038	HSPC071 protein	hi-lo-lo-hi
15	421059	AJ654133	Hs.30212	thyroid receptor interacting protein 15	hi-lo-lo-hi
	446939	AL133353	Hs.16606	CGI-32 protein	hi-lo-lo-hi
	408576 410073	NM_003542 AW408163	Hs.46423 Hs.58488	H4 histone family, member G catenin (cadherin-associated protein), a	hi-lo-lo-hi hi-lo-lo-hi
	450912	AW939251	Hs.25647	v-fos FBJ murine osleosarcoma virai onco	hi-lo-lo-hi
20	434701	AA460479	Hs.321707	KIAA0742 protein	hi-lo-io-hi
	450455	AL117424	Hs.25035	chtoride intracellular channel 4	hi-lo-lo-hi
	451144 427390	AW956103 AI432163	Hs.61712 Hs.268231	pyruvate dehydrogenase kinase, isoerzyme Homo sepiena cDNA: FLJ23111 fis, clone L	hì-lo-lo-hi hi-lo-lo-hi
	451831	NM_001674	Hs.460	activating transcription factor 3	hì-lo-io-hi
25	406776	T16206	Hs.237164	ESTs, Highly similar to LDHH_HUMAN L-LAC	hi-lo-lo-hi
	428157	Al738719	Hs.198427	hexokinase 2	hì-lo-lo-hi
	408096 418203	BE250162 X54942	Hs.83765 Hs.83758	dhydrofolate reductase CDC28 protein kinase 2	hi-lo-lo-hi hi-lo-lo-hi
	449338	H73444	Hs.394	sdrenomedulfin	hi-lo-lo-hi
30	422082	AA016188	Hs.111244	hyoothetical orotein	hì-lo-lo-hi
	407907	Al752235	Hs.41270	procollagen-lyaine, 2-oxoglutarate 5-dio	hi-lo-lo-hi
	418855 419551	AW988813 AW582258	Hs.79428 Hs.91011	BCL2/adenovirus E1B 19kD-interacting pro anterior gradient 2 (Xenepus laevia) hom	hì-lo-lo-hi hi-lo-lo-hi
	434094	AA305599	Hs.238205	hypothetical protein PRO2013	hi-lo-lo-hi
35	443951	F13272	Hs.111334	ferrilin, likht polypeptide	hi-lo-lo-hi
	422975	AA347720 AA369601	Hs.122669	KJAA0264 protein	hi-lo-lo-hi hi-lo-lo-hi
	430314 412664	AA421404	Hs.239138 Hs.346868	pre-B-cell colony-enhancing factor nucleolar protein p40; homolog of yeast	hi-lo-lo-hi
	408089	H59799	Hs.42644	thloredoxin-like	hi-lo-to-hi
40	409690	W45393	Hs.55888	activeting transcription factor 7	hi-lo-to-hi
	442332 408388	A/693251 AF091086	Hs.8248 Hs.44563	Target CAT hypothetical protein	hi-lo-lo-hi hi-lo-lo-hi
	441252	AW360901	Hs.183047	hypothetical protein MGC4399	hi-lo-lo-hi
	433089	X76732	Hs.3184	nucleobindin 2	hi-lo-lo-hi
45	443837	A1984625	Hs.9884	spindle pole body protein	hi-lo-lo-hi
	426108 441181	AA622037 AA416925	Hs.166468 Hs.121078	programmed cell deelh 5 peptidy/proly/ isomersse (cyclophilin)-!	hi-lo-lo-hi hi-lo-lo-hi
	447397	BE247676	Hs.18442	E-1 enzyme	hi-lo-lo-hi
~~	427505	AA361562	Hs.178761	26S prolessome-associated pad1 homolog	hi-lo-lo-hi
50	430287	AW182459	Hs.125759	ESTs, Weakly similar to LEU5_HUMAN LEUKE	hi-lo-lo-hi
	415857 423198	AA866115 M81933	Hs.127797 Hs.1634	Homo sapiens cDNA FLJ11381 fis, clone HE cell division cycle 25A	hl-lo-lo-hi hl-lo-lo-hi
	407687	AK002011	Hs.37558	hypothetical protein FLJ11149	hi-lo-lo-hi
	431374	BE258532	Hs.251871	CTP synthase	hi-lo-lo-hi
55	413273	U75679 Al564739	Hs.75257 Hs.88505	stem-loop (histone) binding protein ESTs	hi-lo-lo-hi
	442799 443881	R64512	Hs.237146	hypothetical protein FLJ12752	hi-lo-lo-hi hi-lo-lo-hi
	416209	AA236776	Hs.79078	MAD2 (mitotic arrest delicient, yeast, h	hi-lo-lo-hi
60	421834	BE543205	Hs.288771	DKFZP586A0622 protein	hi-lo-lo-hi
00	411263 413924	BE297802 AL119964	Hs.69360 Hs.75616	kineein-like 6 (milotic centromere-assoc seladin-1	hi-lo-lo-hi hi-lo-lo-hi
	450598	AF151076	Hs.25199	hypothetical protein	hi-io-io-hi
	439453	BE264974	Hs.6566	thyroid hormone receptor Interactor 13	hì-lo-lo-hi
65	429612	AF062649	Hs.252587	pituitary lumor transforming 1	hi-lo-lo-hi
03	443426 452353	AF098158 C18825	Hs.9329 Hs.29191	chromosome 20 open reading frame 1 epithelial membrane protein 2	hi-lo-lo-hi hi-lo-lo-hi
	419879	Z17805	Hs.93564	Homer, neuronal immediate early gene, 2	hi-lo-lo-lii
	422363	T55979	Hs.115474	replication factor C (activator 1) 3 (38	hi-lo-lo-hi
70	416065	BE267931	Hs.78996	proliferating cell nuclear antigen	hi-lo-lo-hi
70	424308 447519	AW975531 II46258	Hs.154443 Hs.339665	minichromosome maintenance deficient (S. FSTs	hi-lo-lo-hi hi-lo-lo-hi
	437679	NM_014214		incelloi(myo)-1(or 4)-monophosphatase 2	hi-lo-lo-hi
	446636	AC002563	Hs.15767	citron (rho-interacting, serine/threonin	hl-lo-lo-hi
75	422094	AF129535	Hs.272027	F-box only protein 5	hi-lo-lo-hi
75	440334 421921	BE276112 H83363	Hs.7165 Hs.6820	zinc finger protein 259 transfocase of inner mitochondrial membr	hi-lo-lo-hi hi-lo-lo-hi
	422938	NM_001809	Hs.1594	centromere protein A (17kD)	hi-lo-lo-hi
	427719	Al393122	Hs.134726	ESTs	hi-lo-lo-hi
80	422283	AW411307	Hs.114311	CDC45 (cell division cycle 45, S.cerevis	hi-lo-lo-hi
00	424840 418216	D79987 AA662240	Hs.153479 Hs.283099	extra spindle poles, S. cerevisiae, homo AF15q14 prolein	hl-lo-lo-hi hi-lo-lo-hi
	412140	AA219691	Hs.73625	RAB6 Interacting, kinesin-like (rabkines	hi-lo-lo-hi

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	418322	AA284166	Hs.84113	cyclin-dependent kinase inhibitor 3 (CDK	hi-lo-lo-hi
	428479	Y00272	Hs.334562	cell division cycle 2, G1 to S and G2 to	hi-lo-lo-hi
	449722 417933	BE280074 X02308	Hs.23960	cyclin B1	hi-lo-lo-hi
5	433001	AF217513	Hs.82962 Hs.279905	Ihymidylate synthetase clone HQ0310 PRO0310p1	hi-lo-lo-hi hi-lo-lo-hi
-	413943	AW294416	Hs. 144687	Homo sepiens cDNA FLJ12981 fis, clone NT	hi-lo-lo-hi
	424905	NM_002497	Hs.153704	NIMA (never in mitosis gene a)-related k	hi-lo-lo-hi
	422765	AW409701	Hs.1578	baculoviral IAP repeat-containing 5 (sur	hi-lo-lo-hi
10	425397 444371	J04068 BE540274	Hs.156346 Hs.239	lopoisomerase (DNA) II alpha (170kD) forkhead box M1	hi-lo-lo-hi hi-lo-lo-hi
10	422956	BE540274 BE545072	Hs. 122579	ECT2 protein (Epithelial celt transformi	ni-io-io-ni hi-io-io-hi
	444783	AK001468	Hs.62180	anilin (Drosophila Scraps homolog), act	hi-lo-lo-hi
	453884	AA355925	Hs.36232	KIAA0186 gene product	hi-lo-lo-hi
16	416980	AA381133	Hs.80684	high-mobility group (nonhistone chromoso	hi-lo-lo-hi
15	442432 417308	BE093589 H60720	Hs.38178 Hs.81892	hypothetical protein FLJ23468 KIAA0101 gene product	hl-lo-lo-hl hi-lo-lo-hi
	433133	AB027249	Hs.104741	PDZ-binding kinase; T-cell originated pr	hi-lo-lo-hi
	432626	AA471098	Hs.278544	acetyl-Coenzyme A acetyltransferase 2 (a	hi-lo-lo-hi
20	441020	W79283	Hs.35962	ESTs	hi-lo-lo-hi
20	412281	Al810054	Hs.14119	ESTs	hi-lo-lo-hi
	435602 400882	AF217515	Hs.283532	uncharacterized bone marrow protein BM03 Target Exon	hi-lo-lo-hi hi-lo-lo-hi
	446269	AW263155	Hs.14559	hypothelical protein FLJ10540	hi-lo-lo-hi
	417847	Al521558	Ha.7331	hypothelical protein FLJ22316	hi-lo-lo-hi
25	400681			NM_025080tHomo sapiens hypothetical prot	hi-lo-lo-hi
	419356 400292	A/656166 AA250737	Hs.7331 Hs.72472	hypothelicel protein FLJ22316 BMP-R18	hi-lo-lo-hi hi-lo-lo-hi
	415539	AJ733881	Hs.72472	BMP-R1B	hl-lo-lo-hi
	453935	Al633770	Hs.42572	ESTs	hi-lo-lo-hi
30	420005	AW271106	Hs.133294	ESTs	hi-lo-lo-hi
	428450	NM_014791	Hs.184339	KIAA0175 gene product	hi-to-lo-hi
	436291 441362	BE568452 BE614410	Hs.344037 Hs.23044	protein regulator of cytokinesis 1 RAD51 (S. cerevisiae) homolog (E coli Re	hi-lo-lo-hi hi-lo-lo-hi
	428484	AF104032	Hs.184601	solute carrier family 7 (cationic amino .	hi-lo-lo-hi
35	418526	BE019020	Hs.85838	solute carrier family 16 (monocarboxylic	hi-lo-lo-hi
	458809	AW972512	Hs.20985	sin3-associated polypeptide, 30kD	hi-lo-lo-hi
	444984 447342	H15474 Al199268	Hs.132898 Hs.19322	fatly acid desaturase 1 Homo seplens, Similar to RIKEN cDNA 2010	hi-lo-lo-hi hi-hi-lo-lo
	428330	L22524	Hs.2256	metrix metalloprotoinase 7 (metrilysin,	hi-hi-lo-lo
40	428338	AA503115	Hs.183752	microseminoprotein, beta-	hi-hi-lo-lo
	430389	AL117429	Hs.240845	DKFZP434D146 protein	hi-hi-lo-lo
	417318 422545	AW953937 X02761	Hs.240845	ESTa	hi-hi-lo-lo hi-hi-lo-lo
	422545	D30857	Hs.287820 Hs.82353	fibroneclin 1 protein C receptor, endothelial (EPCR)	ni-ni-io-io hi-io-io-io
45	422809	AK001379	Ha.121028	hypothetical protein FLJ10549	hi-lo-lo-hi
	425580	L11144	Hs.1907	galanin	hi-lo-lo-hi
	416836	D54745 AA626509	Hs.80247	cholecystokinin	hi-lo-lo-hi
	434170 427958	AA418000	Hs.122329 Hs.98280	ESTs potassium intermedialo/small conductance	hl-lo-lo-hì hi-lo-lo-hi
50	439706	AW872527	Hs.59761	ESTs, Weakly similar to DAP1_HUMAN DEATH	hi-lo-lo-hi
	450088	AW292933	Hs.254110	ESTs	H-lo-lo-H
	414219	W20010	Hs.75823	ALL1-fused gene from chromosome 1q	hi-lo-lo-hi
	419201 426263	M22324 AI908774	Hs.1239 Hs.259785	alanyl (membrane) aminopeptidase (aminop camitine palmitoyltransferase I, liver	hi-lo-lo-hi hi-lo-lo-hi
55	456236	AF045229	Hs.82280	regulator of G-protein signalling 10	hl-lo-lo-hi
	456607	AJ660190	Hs.106070	cyclin-dependent kingse inhibitor 1C (p5	hi-lo-lo-hi
	408437	AW957744	Hs.278469	lacrimal proline rich protein	hl-lo-lo-hi
	421180 413437	BE410992 BE313164	Hs.258730 Hs.75361	heme-regulated initiation factor 2-alpha gene from NF2/mentingtome region of 22q12	hi-lo-lo-hi hl-lo-lo-hi
60	432415	T18971	Hs.289014	ESTs, Weakly similar to A43932 much 2 p	hi-lo-lo-hi
00	449230	BE613348	Hs.211579	melanoma cell adhesion molecule	hi-lo-lo-hi
	417979	AU077284	Hs.83081	GTP cyclohydrolase i feedback regulatory	hi-lo-lo-hi
	421877	AW250380	Hs.109059	mitochondrial ribosomal protein L12	hi-lo-lo-hi
65	412482 428423	Al499930 AU076517	Hs.334885 Hs.184276	mitochondrial GTP binding protein solute carrier family 9 (sodium/hydrogen	hi-lo-io-hi hi-lo-io-hi
05	422947	AA306782	Hs.122552	G-2 and S-phase expressed 1	hi-lo-lo-hi
	441072	AW275480	Hs.39504	hypothetical protein MGC4308	hi-lo-lo-hi
	415938	BE383507	Hs.78921	A kinase (PRKA) anchor protein 1	hi-lo-lo-hi
70	432278 446651	AL137506 AA393907	Hs.274256 Hs.97179	hypothetical protein FLJ23963 ESTs	hi-lo-lo-hi hi-lo-lo-hi
10	431515	NM_012152	Hs.258583	endolheital differentiation, lysophospha	hì-lo-lo-hi
	445345	AW003850	Hs.12532	chromosome 1 open reading frame 21	hi-lo-lo-hi
	458965	AA010319	Hs.60389	ESTs	hi-lo-lo-hi
75	438321 416783	AA576635 AA206186	Hs.6153 Hs.79889	CGI-48 protein	hi-lo-lo-hi hi-lo-lo-hi
13	453563	AW608906	Hs.181163	monocyte to macrophage differentiation-a hypothetical protein MGC5629	hi-to-to-ni
	432393	AW205863	Hs.133988	hypothetical protein FKSG28	hi-lo-lo-hi
	433914	AF108138	Hs.112160	Homo sapiens DNA helicase homolog (PIF1)	hi-lo-lo-hi
80	414907	X90725 RE536069	Hs.77597 Hs.2962	polo (Crosophia)-like kinase	hi-lo-lo-hi hi-lo-lo-hi
90	432375 440773	BE536069 AA352702	Hs.2962 Hs.37747	S100 calcium-binding protein P Homo sapiens, Similar to FUKEN cDNA 2700	hi-lo-lo-hi hi-lo-lo-hi
	415994	NM_002923	Hs.78944	regulator of G-protein signalling 2, 24k	hi-lo-lo-hi
				174	

	412722		Hs.15091	ESTs	hi-lo-lo-hi
	446839	BE091926	Hs.16244	mitofic spindle coiled-coil related prol	hi-lo-lo-hi
	428862			SRY (sex determining region Y)-box 9 (ca	hi-lo-lo-hi
5	439108		Hs.6467	synaplogyrin 3	hi-lo-lo-hi
)	430178		Hs.152475	ESTs	hi-lo-lo-hi
	421733	AL119671	Hs.1420	fibroblast growth factor receptor 3 (ach	hi-lo-lo-hi
	452410	AL133619		Homo sapiens mRNA; cDNA DKFZp434E2321 (f	hi-lo-lo-hi
	430132	AA204686	Hs.234149	hypothetical protein FLJ20647	hì-lo-lo-hi
10	428297	AA236291	Hs.183583	serine (or cysteine) proteinase inhibito	hi-lo-lo-hi
10	413142	M81740	Hs.75212	ornithine decarboxylase 1	hi-lo-lo-hi
	427239	BE270447	Hs.174070	ubiquitin carrier protein	hì-lo-lo-hì
	409738	BE222975	Hs.56205	insultn Induced gene 1	hi-lo-lo-hi hi-lo-lo-hi
	410748	BE383816	Hs.12532	chromosome 1 open reading frame 21	nHo-Io-III hi-Io-Io-Iii
15	424506	AF220490	Hs.149623	group III secreted phospholipase A2	
13	447333		Hs.70704	hypothetical protein dJ616B8.3	hì-lo-lo-hi
	414761	AU077228	Hs.77256	ennancer of zeste (Drosophila) homolog 2	hi-lo-lo-hi
	419602	AW248434	Hs.91521	hypothetical prolein	hi-lo-lo-hi
	411669	BE612676	Hs.303116	stromal cell-derived factor 2-like 1	hl-lo-lo-hi ht-lo-lo-hi
20	452322	BE566343	Hs.28988	glutaredoxin (thio/transferase)	hi-lo-lo-hi
20	426006	R49031 AW301344	Hs.22627	ESTs	hi-lo-lo-hi
	457465		Hs.122908	DNA replication factor kerstin 19	hi-lo-lo-hi
	406867	AA157857	Hs.182265	keralin 19	ni-lo-lo-lii
	407230	AA157857 AJ003624	Hs.182265 Hs.15896	kendrin	nHo-lo-hi
25	446681	BE206854	Hs.46039	phosphoelyperale mulase 2 (muscle)	hi-lo-lo-hi
23	408493	AI697274	Hs.105435	GDP-mannose 4.6-dehydralase	hi-lo-lo-hi
	439186 424544	M88700	Hs.150403	dopa decarboxylase (aromatic L-amino aci	hi-lo-lo-hi
	431325	AW026751	Hs.5794	ESTs, Weakly similar to 2109260A B cell	hi-lo-lo-hi
	414922	D00723	Hs.77631	givoine cleavage system protein H (amino	hi-lo-lo-hi
30	438291	BE514605	Hs.289092	Homo sapiens cDNA: FLJ22380 fis, clone H	hi-lo-lo-hi
30	418574	N28754	PR-209092	M-phase phosphoprolein 9	hi-lo-lo-hi
	409342	AU077058	Hs.54089	RRCA1 associated RING domain 1	hi-lo-lo-hi
	432734	AA837396	Hs.263925	LIS1-interacting protein NUDE1, rat homo	hi-lo-lo-hi
	432734	BE300298	Hs.5054	CGI-133 protein	hi-lo-lo-hi
35	420309	AW043637	Hs.21766	ESTs, Weakly similar to ALU5_HUMAN ALU S	hi-lo-lo-hi
33	411619	AVV043637 AV418609	Hs.71040	hypothetical protein FLJ20425	hi-lo-lo-hi
	424381	AA285249	Hs.146329	prolein kinase Chk2	hì-lo-lo-hi
	442547	AA306997	Hs.217484	ESTs, Weakly similar to ALU1_HUMAN ALU S	hi-lo-lo-li
	430376	AW292053	Hs.12532	chromosome 1 open reading frame 21	hi-lo-lo-hi
40	434688	AF151103	Hs.112259	T cell receivor gamma locus	hi-lo-lo-hi
70	412330	NM 005100		A kinase (PRKA) anchor protein (gravin)	hi-lo-lo-hi
	452123	Al267615	Hs.38022	FSTs	hi-lo-lo-hi
	424893	AW295112	Hs.153648	Homo saciens cDNA FLJ13303 fis, clone OV	hi-lo-lo-hi
	428057	Al343641	Hs.185798	ESTs	hì-lo-lo-hì
45	431566	AF176012	Hs.260720	J domain containing protein 1	hi-lo-lo-hi
	439979	AW800291	Hs.8823	hypothelical protein FLJ10430	hi-lo-lo-hi
	418836	A)655499	Hs.161712	ESTs	hi-lo-lo-hi
	433757	Al949974	Hs.152670	ESTs	hi-lo-lo-hi
	425236	AW087800	Hs.155223	stanniocatcin 2	hì-lo-lo-hi
50	426215	AW963419	Hs.155223	slanniocalcin 2	hi-lo-lo-hi

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TABLE 2B

WC02098558 [file ///E:/WC02098358.cpc]

Fkey: Unique Eos probeset identifier number CAT number: Gene duster number Accession: Genbank accession numbers

-		ar donadin bio	
	Pkey	CAT Number	Accession
	406660	107294_1	AA525775 AA056342 Al538978 AW975281 AA664986
10	409051	109699_1	A4080912 AA075318 AA083403 AA076594 AA078992 AA084926 AA081881 AA113913 AA113892 AA083821 AA134801 AA082953 AA070343
10			AA062835 AA075419 AA063293 AA071252 AA078900 AA062836 AW974306
	409123 410216	110143_1	AAG63403 AA070823 AA070050 REG61839 AW856963 AW806085
	410451	1184664_1 1204118_1	BE065667 BE065637 AW749002 H73690
	410498	120611 1	AA355749 AA085520 AW966333 AA340319 BE170936
15	411053	1230446.1	AW815061 H71985 AW815072 AW815048 AW815041 AW815047 BE152831 BE152490 BE149043 BE149075 BE149035 BE149067
	411233	1236369_1	AW833793 AW833799 AW833346 AW833371 AW833795 AW833962 AW833667 AW833377
	411283	1237666_1	AV/852754 AV/852897 AW/852757 AW/852617 BE172755 AV/835444
	411701	1254466_1	BE181659 AW890576 AW857638
20	411831	1260400_1	AW994394 AW865900 AW865905 AW865891 AW866014 AW865898
20	412419	1293418_1	AW948630 AW948626 AW948634 AW948616 AW948627 AW948615 AW948631 AW948605 AW948611 AW948610 AW948633 AW948623 AW948628 AW948604 AW948602 AW948607
	412492	130082_1	AW962604 AA368639 AA112257
	412657	1318507_1	AW976165 C04000
	413351	1363660_1	BEG86815 BE086823 R81218 R69229
25	413509	1374313_1	BE145419 BE145433
	413672	1382512_1	BE156536 BE156439 BE156700 BE156449 BE156653 BE156533 BE156524 BE156670 BE156721 BE156723
	415308	1533673_1	F05251 R13748 Z44028 H14747
	415516 416508	1539185_1 1597894_1	F11411 R15237 Z43915 H20760 R39769 T53143 H60012
30	416631	1605019_1	H59466 H93884 N59684
20	416954	163427 1	Al222358 N73390 D61648 AA243520 AA190953
	417314	1666649_1	N68168 N69188 N90450
	418056	171841_1	AA524886 A\V971347 AA211537
35	418259 418574	173388_1	AA215404 A1990909 BE464132 AW271459 N74332 AI262061 N28754 N28747 A1968146 A1979339 AA322671 AA322672 AW955043 A1990326 AA776406 A1016250 AA843678 AW451682 N23137 N23129
33	416074	17690_1	WX0051 A K38748 AA831327 AI925845 AW945895
	419555	1858841	A24446 AA24401
	420811	196677_1	AA807544 AA280648 AI243066 AI022744 AA706288 AA829425 AW452095 AI929317 R19039 AA282024
	421911	208987_1	AL041520 AA300086
40	421974	209807_1	AA301270 AA301379 AA301366
	422128 423028	211994_1 224062 1	AW881145 AA490718 M85637 AA304575 T06067 AA331991 H90946 AA320597 AW954970 BE143680
	423476	22861.1	AL035633 F11793 F11783 H18042 T66089 H29379 R19493 AW134660 Al299437 AL133995 AA057405 N78357 AA917450 A1002692 T09262
		2200121	T65008 H29290 Al200874 AA894415 Al732887 Al791768 Al733447 AA988785 N62128 T09261 AW956936
45	423895	233006_1	AA332215 AA403110 AW965299
	424593	241234_1	AA343729 AA345779 AA344370
	425074 425291	246486_1 249618_1	AA495930 A1470890 H97831 AA350358 BE166712 AA354572 AV/062361 AW613419 AW616041 A(744949
	425980	258778_1	AA36951 AA470999 AA469425
50	426413	266650_1	AA377823 AV/954494 AI022688
	428181	287953_1	AA423976 AA437075 BE006469
	429163	300543_1	AA884786 AW974271 AA592975 AA447312
	429540 430068	305828_1 312849_1	M85776 AA454535 AA456208 H90189 AA464964 M85405 AA947566
55	430103	313089_1	AA45259 AVI997142 AW837144
-	430439	31808 1	AL133561 ALQ41990 AL117481 AL122069 AW459292 A1968826
	431089	327825_1	BE041395 AA491826 AA621946 AA715960 AA666102
	431843	338324_1	AA516420 C14818 C14815 C15161 C15068 D80763 D80656 AW970134 AA543007 D81004 D60184 AI498371 D60382 D60181 C15876
60	432079 432340	341114_1 345248_1	AW972746 AA525323 A1150314 AA534222 AA633532 T81234
00	432676	352582_2	A187366 AA55869 AA618478
	433075	35820 1	NM. 002959 X98248 AA233278 AA846376 AI470560 AI470533 BE327147 AV/291971 AA017125 AI198417 AI365213 AI168442 AI337018
			A1475049 H85459 AA969895 AA888000 AA418326 AA418378 N71981 AL043634 AA426361 AA418275 AA232975 AL036861 BE277220 BE387505
65			N9971D AW375004 AA418268 AL079651 H85743 AW902319 AW605907 AA984366 T92310 AA405425 AA421732 A656841 AV300968
00			AW593416 T92267 BE464032 AW473548 A1859502 BE552306 A1990196 AW518361 A1239559 AW590963 AA018359 A1273737 AL042658 AA411308 AA402610 H38111 AW013931 AW366432 AW752435 AW376124 A129020 A1292121 AA340647 BE613672 BE409674 AA351915
			BE617025 BE019588 AW402692 AW247466 R59233 AA134761 BE254019 BE265105 D63316 BE313080 BE547713 BE536578 BE546749
			AA324105 H17386 BE253377 R87598 H29072 AA39080 BE076629 BE253957 AA532613 BE252486 AW804459 D30966 R87959 AA091632
=0	434280	382816_1	BE005398 AA628622 AA994155
70	434609	38950_1	R76593 AF147390 R76594
	435023	398093_1	A1692552 A1393343 A1800510 A1377711 F24263 AA661876
	436716 436862	425440_1 42814_2	A433540 AA728984 AA804981 A4821940 N67106 A7744264 AA808846 AA643417 AA643416 Z70715
	437576	43892 1	BE514383 AA071273 AW247987 AW673286 BE312102 AW749824 BE071985 AW577383 BE071945 BE072005 AW577355 BE071965 AW239231
75		_	BE072000 BE071960 AW577360 AW749830 AW373020 X97303 AW999522 BE000192 BE562219 BE266655 BE264970
	438869	46651_1	AF075009 R63109 R63068
	438882	466649_1	AA827695 AA833754 AW978946
	438980 439046	467544_1 468133_1	AW502384 A/982587 AA828622 AA947354 AA829680 A/687296
80	439848	477806_1	AW979249 D63277 AA846968
	440151	487109_1	AA868167 F21558 F31418 F35624
	440507	495677_1	H06994 BE147898
			4-4

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WC02098558 [file ///E./WC02098358.cpc]

		509604_1 531432_1	AA973905 AI299883 AA917019 H63235 T90771 AA974603 AI964319 AW340495
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	444290		AA262496 AY648929 AA305356 D61644 D78724
5	444314		Al140497 AW749625 AW749626 AW749644
	445808	65133_1	AV655234 AW966332 AA340239
	447329	71759_1	BE090517 AW\$70792 AW\$54490 AW014965 F27436 AA947336 F15843 H89338 AA563626 F17712 BE546579 AA421821 AA284852 AA477751 AW025245
1.0		722246_1	BE244285 C18429 H42373 AI620706 AI379786 R55439 AW276142
10		752165_1	AI472167 AI990315 R32175
	448489		AI523875 R45782 R45781
	448631	772996_1 77790 1	AI554923 AI902356 BE614081 W01988 AW500790
		9163 1	AL133619 AA68118 AA383064 Al476447 T09430 Al673758 AA524895 Al581345 Al300820 AW498812 AA256162 Al559724 Al685732 AA602400
15	102410	3102_1	A9905-633 A204595 AN/186541 AA157458 A4156269 AA386826 AA431072 AN/1892707 A435410 AN/272464 A1215559 AA522747 R724039 NS5031 A1804128 AN/513621 AA686351 A1026826 AH63388 AA614641 W81604 A1657060 A1214351 AA750140 A1125754 A120813 A1806003 A1656082 A8/07063 A475629 A4050009 A1598409 A1898007 A1522939 AW005008 A4751863 A473014 A1787072 AA468315 A1724130 A1724138
	100111	918078 1	AA426284 AA433997 AI741241 AW043563 AI732741 AI732734 AA437369 AA425820 AA664048 R74130 RF144022 RF143969 RF143915
20	452654		BE004783 BE004947 Al911790
20		1234106 1	BE160229 AW819879 AW820179 AW819882 AW819876 AW820169 BE153201 AW993736 BE152911
		1249138 1	BE 100229 AND 1011 A WASHINGS A AVASTION AND 1002 AND 1000 AND 2010 BE 100201 AND 3037-30 BE 102011 AVASDAR A WASHINGS A AVASTION
	455272		BE148152 BE148133 BE148159 BE148132 AW885107
		1346387 1	BE063853 BE063955 BE063866 BE063705 BE063846 BE061416 BE063844
25	455653	1348742_1	BE154075 BE153973 BE064861 BE153852 BE153847 BE064684 BE153802 BE065075 BE154018 BE064772 BE064842 BE153557 BE153509
	455729	1353792_1	BE072092 BE072106 BE072086 BE072093 BE072103
	455824	1372880_1	BE143703 BE143631 BE143629 BE143702
	455956	1387163_1	BE162704 BE162705 BE162732 BE162702 BE162694
30	456123	1534442_1	R00602 Z42921 F06132
30	457133	29066_1	M54568 NM_004985 Al808924 AL135130 AW242010 AA476848 Al740449 M17097 K03210 M35505 M35504 L00049 Al186585 W35273 X01669 X02825 W23836 Al554920 Al539465 AA425263 AM66981 W21091 T28976 AW977922 BE550180 AW64973 Al148939 AW117295 AA811229
			X02825 W23636 A654920 A639956 AA425263 A469961 W21091 128976 AW977922 BE550180 AW664973 A1148939 AW117295 AA611229 A343010 AA766141 BE219368 N96249 AA280396 AW604574 AA232870 AT70018 AA262948 AW450230 AW362890 AW609417 AW499941
			AA25857 AW380865 AA830647 AA282180 T27386 HR5007 AA861543 AA356548 AA356410 AW880656 AW860647 AW380649
			ASSOCIA AVA74707 AASOSS AAG829S AAG829S AV949SIS AASSI728 N3383 AA411821 AA401640 AV594461 AL120768 AISO0024
35			AW771891 H84567 D51551 AA330460 R14184 AI301629 N64676 AV659699 AI697660 AI004579 AA287927 AW453052 AW601642 AA676681
-			AX337010 AA872481 AA28 1094 AA584243 BE464958 BED49285 AW1679 17 AA843916 AA525301 A1015987 N 25230 A189481 AW173466
			A4937541 A1334416 A676214 A1281159 AA553559 AA582189 AA255527 AW160515 AA670007 H08199 AA808271 AA281015 W47527 AA64925
			A364302 AA699246 R40473 H02312 AA648116 AA342730 AA243624 R99351 R41568 R49696 AA654442 F017 13 AA213685 AA721296 R79833
			H84241 R70668 H85554 AA223758 N95349 A374913 A1306683 AA015609 AA918548 AI453570 AA772321 AI692775 AA195733 AI474563
40			AW873048 Al209133 Al028182 Al374920 AW572607 AA406223 AA833684 T97255 H69138 AA382906 AW119162 N31974 Al890584 N39418
			AA864877 AA679469 BE350651 N41020 A1050915 F00075 AA864878 N26970 AA828898 AW019991 AW796631 AW993262 N48532 BE564662
			AV654063 AI754461 AW945712 C03289 AV655314 AV659070 AV659808 AV660435 H70113 C05323 R91984 H96949 AV658936 AV658879
			H69137 AA384411 AA412584 C02749 W32014 R59168 C05526 BE536017 N24354 AA287991 N80109 F05452 R12740 H08297 AL138354
45			AW020801 BE178443 BE178018 BE178336 BE178369 BE178107 BE178365 BE178215 BE178186 BE178447 BE178352 BE178422 BE178424 BE178043 BE178093 BE178460 BE178356 BE178441 BE178438 BE178467 Al091259 BE177839 BE178094 R28455 BE177844 BE178100
73			BE173043 BE170493 BE170490 BE170500 BE170401 BE177603 BE170407 AMB1239 BE177634 BE17030 BE177634 BE17050 BE177634 BE17050 BE177604 BE17050 BE177634 BE17050 BE177634 BE17050 BE177634 BE17050 BE177634 BE17050 BE177604 BE17050 BE17
			AA095144 N32462 AA281203 AA281183 W47526 W05015 R34165 R35396 T97366 R79640 W25258 R99450 AW368425 BE178196 R26447
			MUSO 199 ROZGO MAZO 1203 MAZO 1103 W 41520 W 000 15 RO4 100 RO30380 197300 K 79040 W 20200 RO9040 M 17300425 DE 17 6 190 K 20447
	457952	44256 1	US5750 AITS2472 AA487379 A4872782 AA487262 R22383 A4865750 R21832 AA593628 AW671869 AA377191 R78814 T27193
50	458956	83645 1	BE220675 AA345621 AA009992

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TABLE 2C

Play: Unique number corresponding to an Eas proteed
Ref. Sequence source. The 7 digit numbers in this ordinan are Geolean's Mortifair [Ci] numbers. Thurshamil et al." refers to the publication entitled The DNA sequence of human echromators 22 Dutables 1 Let al. (1999) <u>Nature</u> 402-494. Strand: Indicated DNA strand from which soons were producted.
Strand: Indicated DNA strand from which soons were producted.
No position: Indicates and production of the second producti

	Pkey	Ref	Strand	Nuposition
10	400481	8439853	Plus	112433-112541
	400501	9796227	Minus	12479-12619
	400713	8118874	Minus	43185-43394
	400769	8131628	Plus	28571-29795
	400769			172644-172765.173085-173200
15		8569994	Plus	
13	400881	2842777	Minus	91446-91603,92123-92265
	400882	2842777	Minus	110431-110708
	400965	7770576	Mnus	173043-173564
	400986	8065497	Minus	63140-63319
	400995	8099094	Plus	141186-141601
20	401093	8516137	Minus	22335-23166
	401178	9438616	Minus	133663-133812
	401192	9719502	Minus	69559-70101
	401209	7712287		
			Plus	164932-165112
25	401405	7768126	Minus	69276-69452,69548-69958
23	401416	7452889	Minus	121456-121626
	401419	7452889	Minus	136389-136508
	401444	8346725	Plus	90895-60994.93070-93213
	401512	7622346	Plus	136399-136557
	401563	8247910	Plus	91395-91763
30	401600	4388746	Minus	27363-27518,28727-28891,29526-29731
50	401750	9828651	Plus	82143-82270,89284-89373,90596-90770,95822-96001,96688-96775,96870-96992,98046-98136
	401757	7239630	Plus	88641-88751
	401839	7656637	Plus	1016-1086,2751-2967,3241-3348,28677-26831
25	401849	7770425	Plus	129375-129483,129597-129720
35	401952	3319121	Minus	53770-53979
	401968	3128781	Plus	29397-29918
	402082	8117478	Minus	190046-190183
	402101	8117697	Plus	134308-134487,135402-135587,136421-136548
	402108	8131852	Plus	3717-3848
40	402163	8568936	Plus	166996-167119
70	402185	8576002	Plus	25486-25639
			Plus	
	402240	7890131		104382-104527,106136-106372
	402249	7704953	Minus	107636-107813,108694-108824,110435-110502,113182-113386
40	402347	8099267	Minus	13714-15440
45	402398	1905896	Pfus .	4426-4648
	402469	9797107	Minus	71268-72351
	402532	9800951	Minus	180240-180558
	402559	9864273	Pfus	33539-33715
	402575	9884830	Minus	109742-109883
50	402602	7239666	Plus	6785-6972.7478-7575
	402758	9213869	Plus	87638-87924
	402786	9715046	Plus	47624-47795
	402807	6456148	Minus	101542-101660,103476-103656
	402810	6010110	Pius	12715-12856,13527-13643
55	402964	9581599	Minus	46624-46784
	403046	3540153	Minus	55707-55859.56369-66511
	403055	8748904	Minus	109532-110225
	403217	7630969	Plus	54039-54163.55427-55623
	403218	7630969	Plus	58039-58149
60	403291	7230870	Plus	95177-95435
00	403328	8469086		
			Minus	120428-120703
	403654	8736093	Minos	28634-28758
	403704	4982546	Minus	8850-8996
	403708	5705981	Minus	134394-134812
65	403725	7534031	Plus	86737-86843
	403739	7630882	Plus	44563-44766.48209-48483.52256-52495
	403740	7630882	Plus	86504-87227
	403745	7652036	Minus	67610-68002
	403746	7652036	Plus	93612-93887
70	403885	7710403	Minus	
70	403893			53259-53524
		7710581	Minus	5435-7846
	403947	7711923	Plus	38657-38817
	404039	8698763	Plus	81889-82011
	404064	3548785	Plus	66713-69175
75	404058	3548785	Plus	99397-101808
	404108	8247074	Minus	63603-64942
	404211	5006246	Plus	185728-185885,194575-194686
	404277	1834458	Minus	91665-91948
	404384	8887028	Minus	38055-38156.42175-42391.43435-43553
80				
80	404407	7329316	Minus	48154-48499
	404489	8113772	Plus	98183-98480
	404527	8152087	Plus	127737-127796,128080-128210,129888-130054,132545-132869

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	404528	8152087	Plus	135325-135486
	404661	9797073	Plus	33374-33675,33769-34008
	404663	9797133	Plus	29885-30514
_	404956	7387343	Plus	55883-56203
5	405011	6139150	Ptus	117359-117612
	405044	7596797	Minus	98903-101141
	405102	8076881	Minus	120922-121296
	405109	8096886	Minus	30301-30518
	405188	6649489	Plus	134573-134678
10	405231	7249032	Minus	109793-109969
	405365	2275192	Minus	119867-120372,120481-120824,121029-121357
	405387	6587915	Minus	3769-3833,5708-5895
	405396	6624129	Minus	89965-90273
	405429	7321905	Minus	51577-51723
15	405435	7408068	Minus	51704-51841,53581-53767
	405446	7582529	Plus	99136-99313
	405503	9211311	Minus	51198-51314
	405525	9558552	Minus	19699-19828
	405529	9581957	Minus	38944-39213
20	405610	5757553	Minus	71907-72080
	405802	5924004	Minus	27743-28264
	405811	4902753	Plus	5128-5248
	406180	7283201	Minus	38923-39107
	406207	5923650	Minus	162607-162800
25	406302	8575868	Plus	168961-169150,169610-169769

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Table 3A shows the Seq ID No, Pkey, ExAcon, UnigeneID, and Unigene Title for all of the sequences in Table 4.

5

Pkey: Unique Eos probesel identifier number
ExAcon: Exemplar Accession number, Genbank accession number
UnigenedD: Uniquen number
Uniquen Tibr: Uniquen gene file
Seq ID No: Seq ID number correlation for those sequences in Table 4

	Pkey	ExApon	UnigeneID	Unigene Title	Seq ID No
10	415539	AI733881	Hs.72472	BMP-R1B	Seq ID No 1 & 2
	448988	Y09763	Hs.22785	gamma-aminobutyric acid (GABA) A recepto	Seq ID No 3-10
	403740			NM_001076*:Homo sapiens UDP glycosyllran	Seq ID No 11 & 12
	408633	AW963372	Hs.46677	PRO2000 protein	Seq ID No 13 & 14
	408660	AA525775		ESTs, Moderately similar to PC4259 femi	Seq ID No 15 & 16
15	409051	AA080912		gb:zn04d03.r1 Stratagene hNT neuron (937	Seq ID No 17
	409123	AA063403		qb:zm04d12.s1 Stratagene corneat stroma	Seq ID No 18
	415787	H01463	Hs.93534	ESTs	Seg ID No 19-21
	415999	AA172179	Hs.294029	ESTs	Seq ID No 22
	416225	AA577730	Hs.188684	ESTs, Weakly similar to PC4259 femilin	Seq ID No 23
20	420757	X78592	Hs.99915	androgen receptor (dihydrotestosterone r	Seq ID No 24 & 25
	429163	AA884766		gb:am20a10.s1 Soares_NFL_T_GBC_S1 Homo s	Seq ID No 26
	429441	AJ224172	Hs.204096	lipophilin B (uleroglobin family member)	Sea ID No 27 & 28
	431099	Y13367	Hs.249235	phosphoinositide-3-kinase, class 2, alph	Seg ID No 29 & 30
	432432	AA541323	Hs.115831	ESTs	Seq ID No 31
25	432435	BE218886	Hs.282070	ESTs	Seq ID No 32 & 33
	432527	AW975028	Hs.102754	ESTs	Seg ID No 34
	435876	AW612586	Hs.160271	G protein-coupled receptor 48	Seq ID No 35 & 36
	438233	W52448	Hs.56147	ESTs	Seg ID No 37-40
	439569	AW602166	Hs.222399	CEGP1 prolein	Seg ID No 41 & 42
30	440819	AI809444	Hs.202108	ESTs	Seq ID No 43
	442832	AW206560	Hs.253569	ESTs	Sag ID No 44
	447342	Al199268	Hs.19322	Homo sapiens, Similar to RIKEN cDNA 2010	Seg ID No 45 & 46
	447499	AW262580	Hs.147674	protocadherin beta 16	Seq ID No 47 & 48
	451411	AA017492	Hs.135655	EST	Seg ID No 49
35	451720	AW970985	Hs.290853	ESTs	Seq ID No 50 & 51

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Table 38 shows the accession sumbers for those Pixey's locking UniquenelT's for table 34. For each probesed is laided gene cleater sumber from which oligorous-beldes were designed. Gene clusters were compiled using secon

5	Pixey	CAT Number A	Acotssion
	408660	107294 1 A	ASSS775 AACSS342 AIS38978 AW975281 AASS4986
	409051	109699_1 A	A080912 A0075318 A0083403 A0076994 A0078992 A0084926 A0081881 AA113913 AA113892 AA083821 AA134801 AA082953 AA070345
		A	A062835 AA076419 AA063293 AA071252 AA078900 AA062836 AW974305

10 499123 110143_1 AA063403 AA070823 AA070050 429163 300543_1 AA884766 AW974271 AA592975 AA447312

WC02098358 [file:///E:/WC02098358.cpd]

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Table 3C shows genomic positioning for those Pkey's leaking Unigene ID's and accession numbers in table 3A. For each prodicted exon is listed genomic sequence source uted for prodiction. Nucleotide locations of each prodicted exon are also listed.

5 Pkey Ref Strand Nt_position 5 403740 7630892 Plus 86504-87227

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Table 4.

Seq ID NO: 1 DNA sequence Nucleic Acid Accession #: NM_001203 Coding sequence: 274..1782

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COCCOOCCC COACTCOCCS GOSCCTCCCS GGACGCOGCC ACTGCGGAGA CCGCGGCGCT 10 GAGGACGCGG GAGCCCGGAG CGCACGCGGG GGGTGGAGTT CAGCCTACTC TTTCTTAGAT 120 OTGARAGGAA AOGAAGATCA TITCATGCCT TGTTGATAAA GGTTCAGACT TCTGCTGATT 180 CATAACCATT TOGCTCTGAG CTATGACAAG AGAGGAAACA AAAAGTTAAA CTTACAAGCC TGCCATAAGT GAGAAGCAAA CTTCCTTGAT AACATGCTTT TGCGAAGTGC AGGAAAATTA 300 AATGTGGGCA CCAAGAAAGA GGATGGTGAG AGTACAGCCC CCACCCCCCG TCCAAAGGTC 250 15 TTGCGTTGTA AATGCCACCA CCATTGTCCA GAAGACTCAG TCAACAATAT TTGCAGCACA 420 CACOGATATT GTTTCACGAT GATAGAAGAG GATGACTCTG GGTTGCCTGT GGTCACTTCT 480 GGTTGCCTAG GACTAGRAGG CTCAGATTTT CAGTGTGGGG ACACTCCCAT TCCTCATCAA AGAAGATCAA TTGAATOCTG CACAGAAAGG AACGAATGTA ATAAAGACCT ACACCCTACA CTGCCTCCRT TGRARRACAG AGATTTTGTT GATGCRCCTA TACRCCRCRG GGCTTTRCTT 660 20 ATATCTGTGA CTGTCTGTAG TTTGCTCTTG GTCCTTATCA TATTATTTTG TTACTTCCGG 720 TATARARGAC AAGRAACCAG ACCTOGATAC AGCATTGGGT TAGAACAGGA TGARACTTAC 780 ATTCCTCCTG GAGAATCCCT CACAGACTTA ATTGAGCAGT CTCAGAGCTC AGGAAGTGGA 840 TCRGGCCTCC CTCTGCTGGT CCANAGGACT ATAGCTRAGC AGATTCRGRT GGTGALACRA ATTGGRARAG GTGCGTRTGG GAAGTTTGG ATTGGGRARAGT GGCTGGCCA ARAGCTRGCT GTGARAGTGT TCTTCRCCAC AGAGGRAGCC AGTGGTTCG GAGGACAGA ARTATTCTG 2.5 1020 ACAGTGTTGA TGAGGGATGA AAACATTTTG GGTTTCATTG CTGCAGATAT CAAAGGGACA 1080 OGGTCCTGGA CCCACTTGTA CCTAATCACA GACTATCATG AAAATGGTTC CCTTTATGAT 1140 TATCTGAAGT CCACCACCT AGACGCTARA TCAATGCTGA AGTTAGCCTA CTCTTCTGTC
AGTGGCTTAT GTCATTTACA CACAGAAATC TITAGTACTC AAGGCAAACC AGCAATTGCC 1266 30 CATCCAGATC TCARRACTERA ARROTTCTC CTCARGARAR ATCCARCTTC CTCTATTCCT 1320 GACCTOGGCC TOGCTOTTAA ATTTATTAGT GATACAAATG AAGTTGACAT ACCACCTAAC 1380 ACTOGRACTE GCACCAAACG CTATATGCCT CCAGAAGTGT TGCACGAGAG CTTGAACAGA 1440 AATCACTICC AGTCTTACAT CATGGCTGAC ATGTATAGTT TIGGCCTCAT CCTTTGGGAG GTTGCTAGGA GATGTGTATC AGGAGGTATA GTGGAAGAAT ACCAGCTTCC TTATCATGAC 1860 35 CTAGTGCCCA GTGACCCCTC TTATGAGGAC ATGAGGGAGA TTGTGTGCAT CAAGAAGTTA CGCCCCTCAT TCCCAAACCG GTGGAGCAGT GATGAGTGTC TAAGGCAGAT GGGAAAACTC 1620 1680 ATCACAGAAT GCTGGGCTCA CAATCCTGCA TCAAGGCTGA CAGCCCTGCG GGTTAAGAAA 1740 ACACTTGCCA ARATGTCAGA GTCCCAGGAC ATTARACTCT GATAGGAGAG GARAGGTAAG 1800 CATCTCTGCA GAAAGCCAAC AGGTACTCTT CTGTTTGTGG GCAGAGCAAA AGACATCAAA TAAGCATCCA CATGACAAGC CTGAACATC GTGCTGCTCTC CGAGTGGGTT CAGACCTCAC CTTCAGGGA GCGACCTGGG CAAAGAAGA GAAGCTCCCA GAAGGAGGA TTGATCCGTG 1860 40 1920 1980 TCTGTTTGTA GGCGGAGAAA CCGTTGGGTA ACTTGTTCAA GATATGATGC AT

45 Seq ID NO: 2 Protein sequence Protein Accession #: NP 001194

31 41 MLLRSAGKLN VGTKKEDGES TAPTPRPKVL RCKCHHHCPE DSVMNICSTD GYCFTMIEED 50 DSGLPVVTSG CLGLEGSDFQ CRDTPIPHQR RSIECCTERN ECNKOLHPIL PPLKWRDFVD GPIHHRALLI SVTVCSLLLV LIILPCYFRY KRQETRPRYS IGLEQDETYI PPGESLRDLI 120 180 EQSQSSGSGS GLPLLVQRTI AKQIQMVKQI GKGRYGEVWM GKWRGEKVAV KVFFTTEBAS 240 WFRETEIYOT VLMRHENILG FIAADIKGTG SWTQLYLITD YHENGSLYDY LKSTTLDAKS 300 MLKLAYSSVS GLCHLHTEIF STOGKPAIAH RDLKSKNILV KKNGTCCIAD LGLAVKFISD 3 60 55 MEKLAYSYS GLCHENTER SYGGKFALAN KOLKSYNILV KYMSTCCIAD LGLAVKFISD TNEVDIPPNT RYGTKRYMPP EVLDESLNEN HFGSYIMADM YSPGLILMEV ARRCYSGGIV EEYALPYHDL VPEDPSYEDM REIVCIKKER PSPPNRNSSD RCHROMKEM TECHANNDAS RITALRYKKT LAKMSESODI KL

60 Seq ID NO: 3 DNA sequence Mucleic Acid Accession #: NM_004961.2 Coding sequence: 55..1575

GCCAGAGCET GACCOCCAC CTCCCCCCAG GTGGTCCCCC GGGTCTCCCC GGAAATUTTG TCCAAACTC TTCCAGTCCT CCTAGGCAC TTATGCATC TCCAGTGGAG GGTCGAGGAC CCTCAGACTG AATCAAAGAA TGAAGCCTCT TCCCGTGATG TTGTCTATGG CCCCCAGCCC CAGCCTCTGA GAAATCAGCT CTCTCTGGG GAAACAAAGT CTACTGAGGAC TGGACCTGGG CAGCCTCTGG AAAATCAGCT CTCTCTGGG GAAACAAAGT CTACTGAGGAC TGGACCTGGG 65 120 180 240 ACCAGACTTG GCAAACTGCC AGAAGCCTCT COCATCCTGA ACACTATCCT GACTAATTAT 70 GACCACARAC TECSCOCTOS CATTEGAGAS AAGCCCACTS TEGTCACTOT TEMENTOGCC STCAACAGCC TIGSTCCTCT CICTATCCTA GACATEGAAT ACACCATTGA CATCATCTTC 360 420 TOCCAGACCT GOTACGACGA ACGCCTCTGT TACAACGACA CCTTTGAGTC TCTTGTTCTG 480 AATGGCAATG TGGTGAGCCA GCTATGGATC CCGGACACCT TTTTTAGGAA TTCTAAGAGG 540 ACCCACGAGO ATGAGATCAC CATGCCCAAC CAGATGGTCC GCATCTACAA GGATGGCAAG CHOPTOTACA CANTIAGGAT GACCATTGAT GCCGGATGCT CACTCCACAT GCFCAGATTT c c 0 CCAATGGATT CTCACTCTTG CCCTCTATCT TTCTCTAGCT TTTCCTATCC TGAGAATGAG 720 ATGATCTACA ACTGGGAAAA TTTCAAGCTT GAAATCAATG AGAAGAACTC CTGGAAGCTC TTCCAGTTTG ATTTTACAGG AGTGAGCAAC AAAACTGAAA TAATCACAAC CCCAGTTGGT GACTTCATGG TCATGACGAT TTTCTTCAAT CTGAGCAGGC GGTTTGGCTA TGTTGCCTTT 900 80 CARACTATG TCCCTTCTTC CGTGACCAGG ATGCTCTCCT GGGTTTCCTT TTGGATCAAG 960 ACAGAGTOTG CTCCAGCCCG GACCTCTCTA GGGATCACCT CTGTTCTGAC CATGACCACG 1020 TTGGGCACCT TTTCTCGTAA GAATTTCCCG CGTGTCTCCT ATATCACAGC CTTGGATTTC 1080 TATATOSCCA TOTOCTTOST CTTCTGCTTC TGCGCTCTGT TGGAGTTTGC TGTGCTCAAC

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	TTCCTGATCT	ACAACCAGAC	AAAAGCCCAT	GCTTCTCCTA	AACTCCGCCA	TCCTCGTATC	1200
	AATAGCCGTG	CCCATGCCCG	TACCOGTGCA	CCTTCCCGAG	CCTGTGCCCG	CCAACATCAG	1260
	GAAGCTTTTG	TGTGCCAGAT	TGTCACCACT	GAGGGAAGTG	ATGGAGAGGA	GCGCCCGTCT	1320
-	TGCTCAGCCC	AGCAGCCCCC	TAGCCCAGGT	AGCCCTGAGG	GTCCCCGCAG	CCTCTGCTCC	1380
5	AAGCTGGCCT	GCTGTGAGTG	GTGCAAGOGT	TTTAAGAAGT	ACTTCTGCAT	GGTCCCCGAT	1440
	TGTGAGGGCA	GTACCTGGCA	GCAGGGCCGC	CTCTGCATCC	ATGTCTACCG	CCTGGATAAC	1500
	TACTCGAGAG	TTGTTTTCCC	AGTGACTTTC	TTCTTCTTCA	ATGTGCTCTA	CTGGCTTGTT	1560
	TGCCTTAACT	TGTAGGTACC	AGCTCGTACC	CTGTGGGGGCA	ACCTCTCCAG	TTCCCCAGGA	1620
4.0	GGTCCAAGCC	CCTTGCCAAG	GGAGTTGGGG	GAAAGCAGCA	GCAGCAGCAG	GAGCGACTAG	1680
10	AGTTTTTCCT	GCCCCATTCC	CCAAACAGAA	GCTTGCAGAG	GGTTTGTCTT	TGCTGCCCCT	1740
	CTCCCCTACC	TESCCCATTC	ACTGAGTCTT	CTCAGCAGAC	CATTTCAAAT	TATTAATAAA	1800
				COGTGATGCT			1860
				TANGTACAGG			1920
4.0				TTCCACAAGC			1980
15				ACTGCACCGA			2040
				TAACAGGAGG			2100
				CTGCTACCCC			2160
				GGGCAGCAAG			2220
20				CTCTCCTTGC			2280
20				GTATCTATTT			2340
				TTCTCTTTGA			2400
				CCAGGCACTA			2460
				ACAGGCATTA			2520
25				TTGCTTGACC			2580
25				ACAATCAATC			2640
				TTGACAAGTT			2700
				TCTTATCCCC			2760
				TCACTGGAAG			2820
20				GCTCAGTTCA			2880
30				AATGGCGACC			2940
				CARATCICTC			3000
				ATATGCTAAG			3060
				TCTACTTTTT		TCTGAAATGG	3120
25	GGAAATATGT	AAATAAATAT	ATCAGCAAAG	CAAAAAGAAA	аллаалла		

Seq ID NO: 4 Protein sequence Protein Accession #: NP_004952.1

35

40	1	11	21 	31 	41 	51 	
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	TGSRVGKLPE	ASRILNTILS	NYDHKLRPGI	GEKPTVVTVE	IAVNSLGPLS	ILDMEYTIDI	120
	IFSQTWYDER	LCYNDTFESL	VLNGNVVSQL	WIPDTFFRMS	KRTHEHEITM	PHQMVRIYED	180
		IDAGCSLHML					240
45		SNKTEIITTP					300
		SLGITSVLTM					360
		AHASPKLRHP					420
		PGSPEGPRSL		KRFKKYFCMV	PDCEGSTWQQ	GRLCIHVYRL	480
50	DNYSRVVFPV	TFFFFFNVLYN	LVCLNL				

Seq ID NO: 5 DNA sequence Mucleic Acid Accession #: NM_021984.1

		Coding sequ	lence: 572.	1753				
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		TCCAAAGTTC	TTCCAGTCCT	CCTAGGCATC	TTATTGATCC	TCCAGTCGAG	AACATGTATA	120
		CAGAGAAGTG	CTCARATCAT	AAGTGTACAG	CTGATGAGTT	GTCARARAAT	GACCACAGCG	180
- (60	GTGTAAAGAA	AGCCAAATCA	AGGACCCGAA	TGTGAGCAGG	ACCTCAGAAG	CCCCCTTTGT	240
		CACTGCCTCC	CAGCAAAGGC	AGCACTATCC	GGACTTCTAA	CACCATCGGG	TOGAGGGACC	300
		TCAGACTGAA	TCAAAGAATG	AAGCCTCTTC	CCGTGATGTT	GTCTATGGCC	CCCAGCCCCA	360
		GCCTCTGGAA	AATCAGCTCC	TCTCTGAGGA	AACAAAGTCA	ACTGAGACTC	AGACTGGGAG	420
				AAGCCTCTCG				480
- (55	CCACAAACTG	CGCCCTGGCA	TTGGAGAGAA	GCCCACTGTG	GTCACTGTTG	AGATCTCCGT	540
				CTATCCTAGA				600
				GCCTCTGTTA				660
		TOGCAATGTG	CTCACCCAGC	TATGGATCCC	GGACACCTTT	TTTAGGAATT	CTAAGAGGAC	720
	=0	CCACGAGCAT	GAGATCACCA	TGCCCAACCA	GATGGTCCGC	ATCTACAAGG	ATGGCAAGGT	780
	70	GTTGTACACA	ATTAGGATGA	CCATTUATGC	CGGATGCTCA	CTCCACATGC	TCAGATTTCC	840
				CTCTATCTTT				900
				TCAAGCTTGA				960
				TGAGCAACAA				1020
				TCTTCAATGT				1080
	75			TGACCACGAT				1140
				CCTCTCTAGG				1200
				ATTTCCCGCG				1260
				TCTGCTTCTG				1320
	20			AAGCCCATGC				1380
-	80			OCCUTOCACG				1440
				TCACCACTGA				1500
				GCCCAGGTAG				1560
				CCARCCCTTT				1620

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Seq ID NO: 6 Protein sequence Protein Accession #: NP_068819.1

35	1 MRYTIDIIPS	11 OTWYDERLCY	21 NOTPESIVIN	31 GNUVSOLWIP	41 DTFFRNSKRT	51 HEHEITMPNO	6
40	MVRIYKDGKV INEKNSWKLF LSWVSFWIKT ALLEFAVLNF GSDGEERPSC	LYTIRMTIDA QLDFTGVSNK	GCSLHMLRFP TEIITTPVGD ITSVLTMTTL SPKLRHPRIN PEGPRSLCSK	MDSHSCPLSF FMVMTIFFNV GTFSRKNFPR SRAHARTRAR LACCBUCKRF	SSFSYPENEM SRRFGYVAFQ VSYITALDFY SRACARQHQB	IYKWENFKLE NYVPSSVTTM IAICFVFCFC AFVCQIVTTE	124 244 306 366

45 Seq ID NO: 7 DNA sequence Nucleic Acid Accession #: NM_021987.1 Coding sequence: 572..1657

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	CAGAGAAGTG	CTCAAATCAT	AAGTGTACAG	CTGATGAGTT	GTCAAAAAAT	GACCACAGCG	180
	GTGTAAAGAA	AGCCAAATCA	AGGACCCGAA	TGTCAGCAGG	ACCTCAGAAG	CCCCCTTTGT	240
	CACTGCCTCC	CAGCAAAGGC	AGCACTATCC	GGACTTCTAA	CACCATCG3G	TCGAGGGACC	300
55		TCAAAGAATG					360
		AATCAGCTCC					420
		AAACTGCCAG					480
		CGCCCTGGCA					540
c0		GGTCCTCTCT					600
60		AATTCTAAGA					660
		AAGGATGGCA					720
		ATGCTCAGAT					780
		CCTGAGAATG					840
		TCCTGGAAGC					900
65		ACCCCAGTTG					960
		TATGTTGCCT					1020
		TTTTGGATCA					1080
		ACCATGACCA					1140
70		GCCTTGCATT					1200
70		GCTGTGCTCA					1260
		CATCCTCGTA					1320
		CGCCAACATC					1380
		GAGCGCCCGT					1440
70		AGCCTCTGCT					1500
75		ATGGTCCCCG					1560
		CGCCTGGATA					1620
		TACTGGCTTG					1680
		AGITCCCCAG					1740
80		AGGAGCCACT					1800
80		TTTGCTGCCC					1860
		ATTATTAATA					1920
		AAAACCACAG					1980
	GGCGGGATTAG	CTATCTTCCA	ACAATGCTGA	CCACCAGACA	ATTACTGCAT	TTTTCCAGAA	2040

	GCCCACTATT	GCCTTTGCAG	TGCTTTCGGC	CCAGTTCTGG	CCTCAGCCTC	AAAGTGCACC	2100
	GACTAGTTGC	TTGCCTATAC	CTGGCACCTC	ATTAAGATGC	TGGGCAGCAG	TATAACAGGA	2160
	GGAAGAGATC	CCTCTCCTTT	GCTCAGATTA	TTATGTTCTC	AGTTCTCTCT	CCCTGCTACC	2220
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5	AGAGAGCCTA	TTTGGGACAG	CATTCCTCTC	TCTCTGCTGC	TGTGACATCT	CCCTCTCCTT	2340
	GCTGGCTCCA	TCTTTCGTCT	GCACTACCAA	TTCAATGCCC	TTCATCCAAT	GGGTATCTAT	2400
	TTTTGTGTGT	GATTATAGTA	ACTACTCCCT	GCTTTATATG	CCACCCTCTT	CCTTCTCTTT	2460
	GACCCCTGTG	ACTOTTTCTG	TAACTTTCCC	AGTGACTTCC	CCTAGCCCTG	ACCAGGCACT	2520
	AGGCCTTGGT	GACTTCCTGG	GGCCAAGAAA	CTAAGGAAAC	TCCCCTTTCC	AACAGGCATT	2580
10	ACTCGCCATT	GATTGGTGCC	CACCCAGGGC	ACACTGTCGG	AGTTCTATCA	CTTGCTTGAC	2640
		ATAAACCAGT					2700
		CCCTTAAATT					2760
		TGGAGCTTCA					2820
1.		ATGAAAACCC					2880
15	GCTATCCAAG	AGCCCACTGT	CACCTTCTAG	ACCACATGAT	AGGGCTAGAC	AGCTCAGTTC	2940
		TCTTCTGTCA					3000
		CTCAATTTCT					3060
		GTAACCCAGT					3120
••		TGTCTGTAAT					3180
20	TGTCACCATC	ATCTGAAATG	GGGAAATATG	TAAATAAATA	TATCAGCAAA	GC	
	Daw ID MO.	8 Protein :	amianca				
		ession #: 1					
	Process Acc	design #					

25	1	11	21	31	41	51	
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		QTWNSKRTHE					60
		FSYPENEMIY					120
	VMTIFFNVSR	REGYVAEQNY	VPSSVTTMLS	WVSFWIKTES	APARTSLGIT	SVLTMTTLGT	180
30	FSRKNFPRVS	YITALDFYIA	ICFVFCFCAL	LEFAVLNFLI	YNOTKAHASP	KLRHPRINSR	240
		ACARQHQEAF					300
	CCEWCKRFKK	YFCMVPDCEG	STWQQGRLCI	HVYRLDNYSR	VVFPVTFFFF	NAPAMPACTN	360

35 Seq ID NO: 9 DNA sequence Nucleic Acid Accession #: NM_021990.1 Coding sequence: 1309..2490

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		TGTGGTGCAT					420
		CTGTCTGTGG					480
60		AGCCTCCTTC					540
50		ANANCOGCAN					600
		TECTETCAGE					660
		TAGAGGCCAA					720
		TTCATTTCAC					780
~ ~		AATAAAAGAG					840
55		TTAAAGAAAT					900
		TTTAACTAGG					960
		CTGGGGCCCC					1020
		AGGGACCTCA					1080
60		AGCCCCAGCC					1140
00		CTGGGAGCAG					1200
		ATTATGACCA					1260
		TCTCCGTCAA					1320
		TCTTCTCCCA					1380
65		TTCTGAATGG					1440
03		AGAGGACCCA					1500
		GCAAGGTGTT					1560
		GATTTCCAAT					1620
		ATGAGATGAT					1680
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70		TTGGTGACTT					1800
		CCTTTCARAR					1860
		TCAAGACAGA					1920
		CCACGTTGGG					1980
75		ATTTCTATAT					2040
13	TTTGCTGTGC	TCAACTTCCT GTATCAATAG	GATCTACAAC	CAGACAAAAG	CCCATGCTTC	TCCTAAACTC	2160
		ATCAGGAAGC					2220
		CGTCTTGCTC					2280
80							2340
00		CCGATTGTGA					2460
		TTGTTTGCCT					2520
		CAGGAGGTCC					2520
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	AGCAGGAGCG	ACTAGAGITT	TTCCTGCCCC	ATTCCCCAAA	CAGAAGCTTG	CAGAGGGTTT	2640
	GTCTTTGCTG	CCCCTCTCCC	CTACCTGGCC	CATTCACTGA	GTTTTCTCMG	CAGACCATTT	2700
_	CAAATTATTA	ATAAATGGGC	CACCTCCCTC	TTCTTCAAGG	AGCATCCGTG	ATGCTCAGTG	2760
	TTCAAAACCA	CAGCCACTTA	GTGATCAGCT	CCCTAAAACC	ATGCCTAAGT	ACAGGCGGAT	2820
5		CCAACAATCC					2880
	ATTGCCTTTC	CACTCCTTTC	OGCCCAGTTC	TGGCCTCAGC	CTCAAAGTGC	ACCGACTAGT	2940
	TGCTTGCCTA	TACCTGGCAC	CTCATTAAGA	TGCTGGGCAG	CAGTATAACA	GGAGGAAGAG	3000
		TTTGGTCAGA					3060
		ATAGACACTG					3120
10		CACCATTOCT					3180
	CCATCITICG	TCTGCACTAC	CAATTCAATG	CCCTTCATCC	AATGGGTATC	TATTTTTTTT	3240
	TGTGATTATA	GTAACTACTC	CCTGCTTTAT	ATGCCACCCT	CTTCCTTCTC	TTTGACCCCT	3300
	CTGACTCTTT	CTGTAACTTT	CCCAGTGACT	TCCCCTAGCC	CTGACCAGGC	ACTAGGCCTT	3360
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15		GCCCACCCAG					3480
		AGTCCACTGT					3546
		ATTTGTATGG					3600
		TCATGATAGC					3660
		CCCTGAGTCA					3720
20		TGTCACCTTC					3780
		TCACCTCTGC					3840
		TCTGGGCCTG					3900
		AGTGGAATGA					3960
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Seq ID NO: 10 Protein sequence Protein Accession #: NP 068830.1

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			GCSLHMLRFP				120
			TEIITTPVCD				180
35			ITSVLTMTTL				240
	ALLEFAVLNF	LIYNQTKAHA	SPKLRHPRIN	SRAHARTRAR	SRACARQHQE	AFVCQIVTTE	300
			PEGPRELCSK		KKYFCNVPDC	EGSTWQQGRL	360
	CIHVYRLDNY	SRVVFPVTFF	FFNVLYWLVC	LNL			

40 Seq ID NO: 11 DNA sequence
Nucleic Acid Accession #: NM_001076.1
Coding sequence: 22..1614

	coursel sedi	dence: 22	.0.4				
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			TICTACTOTT				240
50			TITAACTAAA				300
			TGTTTCAAAA				360
			TTATGACTAC				420
			ACTACAAGAG				480
			ACTOGCTGRA				540
55			ATTTGAGAAG				600
			AGAATTAAGT				660
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			AACCTATTGG				840
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	CTGTACAAGT	CCTTACCCCA	GAATGACCTT	CTTGGTCATC	CCAAAACCAA	AGCTTTTATA	1140
65	ACTCATGGTG	GAACCAATGG	CATCTATGAG	GCGATCTACC	ATGGGATCCC	TATGGTGGGC	1200
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			CATGTCAAGT				1320
			AGAGAATOTO				1380
	CCAATGAAGC	CCCTGGATCG	AGCAGTCTTC	TGGATTGAGT	TTGTCATGCG	CCACAAAGGA	1440
70			AGCTCACAAC				1500
	GTGATAGCAT	TCCTCCTGGC	CTGCGTGGCA	ACTGTGATAT	TTATCATCAC	ARARTTTTGC	1560
	CTCTTTTCTT	TCCGAAAGCT	TGCCAAAACA	GGAAAGAAGA	ACARARGAGA	TTAGTTATAT	1620
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	TTTTAAATGC	AGGATTTCCT	TTTTCCTGTG	ACAAAACATC	TTTTCACAAC	TTACCTTGTT	1740
75	AAGACAAAAT	TTATTTTCCA	GGCATTTAAT	ACGTACTITA	GTTGGAATTA	TTCTATGTCA	1800
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	ATCTTAAATC	ACGAGTTACT	GGATGCAGCA	CGCAACATGG	CACATGTGTA	TACATATGTA	1920
	GCTAACCCTT	COTTOTGCAC	ATCTACCCTA	AAACTTAAAG	TATAATTTAA	AAAAAGCAAA	1980
	TARRARARAT	ACCAACTCTT	TTTTTTAAAC	CAGGAAGGAA	AATGTGAACA	TGGAAACAAC	2040
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Seq ID NO: 12 Protein sequence Protein Accession #: NP_001067.1

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MSLEWTSUFL LIGHSCYPSS GSCGKVLVWP TEYSHWIMMK TILERLYORG HEVTVLTSSA STE/MASKSS AIKLEVYPTS LTXNDLEDSL LKILDRWIYG VSKWTPWSYF SOLORLCWEY 120 YDYSNKLCKD AVLNKKLMMK LOESKFDVIL ADALMPCGEL LAELFWIPFL YSLRFSVGYT 180 FEXNGGGFLF PPSYVPVVNS BLSDOMIFNE RIKNMIHNLY FDFWFOIYDL KKWDOFYSEV 240 LGRPTTLFET MGKARMMLIR TYWDFEFPRP FLPNVDFVGG LHCKPAKPLP KEMERPVOSS 300 GENGIVVPSL GSMISNMSEE SANMIASALA QIPQKVLWRF DGKKPWTLGS NTRLYKWLPQ 360 10 NDLLGEPKTK AFITEGGING IYEAIYEGIP MVGIPLFADQ HDNIAHMKAK GAALSVDIR 420 MSSEDIJINAI, KSUTEDDUVK ENVMKLSETH HOOPMEDIDE AVENTERUME HKCAKHIJEVA 480 AHNLTWIQYH SLOVIAFLLA CVATVIFIIT KFCLFCFRKL AKTCKKKKRD Seq ID NO: 13 DNA sequence Nucleic Acid Accession #: NM 014109.1 Coding sequence: 651..1739 20 CTGTCATTCA TGCTTTGGAA AAGTTTACTG TATATACATT AGACATTCCT GTTCTTTTTG GAGTTAGTAC TACATCCCCT GAAGAACAT CTGCCCAGGT GATTCGTGAA GCTAAGAGAA 120 CAGCACCAAG TATAGTGTAT GTTCCTCATA TCCACGTGTG GTGGGAAATA GTTGGACCGA 180 CACTTAGAGC CACATTTACC ACATTATTAC AGAATATTCC TTCATTTGCT CCAGTTTTAC TACTTGCAAC TTCTGACAAA CCCCATTCCG CTTTGCCAGA AGAGGTGCAA GAATTGTTTA 300 25 TCCGTGATTA TGGAGAGATT TTTAATGTCC AGTTACCGGA TAAAGAAGAA CGGACAAAAT 260 TTTTTGAAGA TTTAATTCTA AAACAAGCTG CTAAGCCTCC TATATCAAAA AAGALAGCAG 420 TTTTGCAGGC TTTGGAGGTA CTCCCAGTAG CACCACCACC TGAGCCAAGA TCACTGACAG 480 CAGAAGAAGT GAAACGACTA GAAGAACAAG AAGAAGATAC ATTTAGAGAA CTGAGGATTT 540 TCTTAAGAAA TGTTACACAT AGGCTTGCTA TTGACAAGCG ATTCCGAGTG TTTACTAAGC 30 CTGTTGACCC TGATGAGGTT CCTGATTATG TCACTGTAAT AAAGCAACCA ATGGACCTTT 660 CATCTGTAAT CAGTAAAATT GATCTACACA AGTATCTGAC TGTGAAAGAC TATTTGAGAG ATATTGATCT AATCTGTAGT AATGCCTTAG AATACAATCC AGATAGAGAT CCTGGAGATC 720 780 GTCTTATTAG GCATAGAGCC TGTGCTTTAA GAGATACTGC CTATGCCATA ATTAAAGAI AACTIGATGA AGACTITGAG CAGCICTOTG AAGAAATTCA GGAATCTAGA AAGAAATGCA GTIGTAGGCC CICCAAATAT GCCCCGTCIT ACTACCATGT GATGCCAAGG CAAAATTCCA CICTITOTTGG TGATAAAGAG TCGAGCCCG AGCCGAATGA AAAGCCGAGTA 900 35 DEC 1,020 CTCCTGTGGC TTGCAGCACT CCTGCTCAGT TGAAGAGGAA AATTCGCAAA AAGTCAAACT 1080 GGTACTTAGG CACCATAAAA AAGCGAAGGA AGATTTCACA GGCAAAGGAT GATAGCCAGA ATGCCATAGA TCACAAAATT GAGAGTGATA CAGAGGAAAC TCAAGACACA AGTGTAGATC 1200 40 ATAATGAGAC COGAAACACA GGAGAGTCTT COGTGGAAGA AAATGAAAAA CAGCAAAATG 1260 CCTCTGAAAG CAAACTGAA TIGAGAATA ATTCAARTAC TIGTAATATA GAGAATGAG TIGAAGACTC TAGGAAGACT ACAGCATGTA CAGAATTGAG AGACAAGATT GCTTGTAATG 1320 1380 GAGATGCTTC TAGCTCTCAG ATAATACATA TTTCTGATGA AAATGAAGGA AAAGAAATGT 1440 CTGTTCTGCG AATGACTCGA GCTAGACOTT CCCAGGTAGA ACAGCAGCAG CTCATCACTG 45 TTGARARGGC TTTGGCARTT CTTTCTCAGC CTACACCCTC ACTTGTTGTG GATCATGAGC 1560 GATTARARA TETTTTGAM ACTSTTGTTA ARABASTCA ARACTACRAC ATATTTCAGT TSGARARITT GTATGCAGTA ATCAGCCARI STATTTATCS GCATGCCARS GACCATGATA ARACATCACT TATTCAGRAR ATGGRGCARS AGGTAGRARA CTTCAGTTGT TCCAGATGAT 1620 1680 GATGICATGO TATCGGGTAT TCTTTATATT CAGTTCCTAT TTAAGTCATT TITGTCATGT CCGCCTAATT GATGAGTAT GAAACCCTCC ATCTTTAAGG AAAAGATTAA AATAGTAATA TAAAAGTATT TAAACTTTCC TGATATTTAT GTACATATTA AGGTAAAATGT CATCTGTAAG 1800 50 1800 1920 ATAACTGATA AATA Seq ID NO: 14 Protein sequence 55 Protein Accession #: NP_054828.1 11 21 2.1 41 51 MDLSSVISKI DLHKYLTVKD YLRDIDLICS NALBYNFDRD PGDRLIRHRA CALRDTAYAI 60 IKEELDEDFE OLCEEIOESE KKRGCSSSKY APSYYHVMPK ONSTLUGDKE SDPEQNEKLK TPSTPVACST PAGLERKIRK KSHWYLGTIK KRRKISQAKD DSQNAIDHKI ESDTEBTQDT 180 SVDENETOKT GESSVEENEK QQNASESKLE LRENSHTCHI ENELEDSRET TACTELROKI ACNGASSSQ ITHISDENEG KENCULRYET ARRSQVEQOO LITVEKALAI LSQPTPSLVV DEERLENLLK TUVKKSQNYN IPQLENLYAV ISQCIYRHEK DEDKTSLIQK MRQEVENPSC 240 300 65 Seq ID NO: 15 DNA sequence Nucleic Acid Accession #: AK001536 70 31 TATATORICA CONTINUADA BATCACONOT BACCACTOTO COMORCACO CONCACONO CAGAACTCTC TTTCTGCATA GTTGAAGACC CCTCTTCACA CAAGATGGTA GCAACAAATC 120 ATAGGTGCAA TTGCACCAAA TTCACAGAAG ATCAATTGAA AATCCTCATC AATACCTTCA 75 CTCAAAAACC TTACCCAGGT TATGCTACCA AACAAAACT TGCTTTAGCA ATCAATGCAG AAGAGICCAG AATCCAGATT TGGTTTCAGA ATCAAAGAGC TAGGCATGGA TTCCAGAAAA 300 CACCAGNACC TGACTITAGA TITAAGCCAC AGCCATOGAC AAGATTAACC TGGTGTGGAG TITCAANATA GAAAGCCAG ATGGGTGTGT ACCACCATA GCACCTITCA ATTACACACA ATCATCCATG CATTATGAA AAACCCATAC CCTGGGATG ATTACAGCAG 360 420

GAAGAARTG GTOCTICAGA GTCAAGAGTC CAAATTTGGT TCCAAAATCA AAGATCTAGA TITCATCICC AGAGAAAAG AGAACCTOIT ATOTCCITAG AATGAGAAGA CCAGAGAAGA

CCAGGGGCAA GGTTTCTGAG GGACTTCAAG GTACAGAAGA TACACAAAGT GGCACCAGCC

TCACTAGCAC TCTCATTCT CAAGAGCCAG AACATGGTGA ATACAGTCAA GTTCAGTGTA

480

600

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	TTTGATAATA	TCAATTTGGG	CCCCAAATCT	CTCTCACAGT	CTTCCTGGGA	GTCTATTCTT	780
	CTTCCAAAAG	TOCAAGCTAA	GCCTTCTGAA	GATGGTAAAC	AACTTGGCCG	GGTGTGGTGG	840
	CTCATGCCTG	TAATCCCAGC	ACTITAGGAG	GCTGAGGCTG	GAAGATTGCT	TGAGCCTAGG	900
_	AGTTTGAAAC	CAGTCTGAGC	AACATAGTAA	GACCCTGTCT	CTATTCTAAA	AAACAAAATA	960
5	AGTAAAAAGG	ACTGTAGGAG	GCCAAGACAG	GTACAGGAGG	CACCACACTA	CCCTGTTGAC	1020
	ACAGCCTGGA	TCCAGAGTTC	AGCAGACCTT	GAGACAATGA	AAACAAACTT	AGTAATAATC	1080
	ATTTTTCAAT	CATTGCAGTA	ATTATTGATT	TGGACAAAAA	TCAATTGACG	TCAAAACCTT	1140
	AAAGTGACGT	TTCTCTGCCT	ATGGAGTGGT	CATTCTTTTA	TTCCTTTAGT	TTCATAATAA	1200
4.0	ATTITCTTT	ACTTAAAAAA	ACTTATAGTT	TGATGAAGAG	TGAGATATAT	ACCTCATCTC	1260
10		CACACA CACA					1320
		CCAACTCCAC					1380
	CAAACCAATG	TGAGATGATT	CCTGATATGA	TACACTAAAA	ACCCCACTGT	CTCTTCTGCA	1440
		AAAAAGTGGG					1500
		CAAGTTGACA					1560
15		ACTCAGGAGG					1620
	AGCCTGGGCA	ACATCATGCG	ACCCCATCTC	TAAAAACATC	TTTTTAAAAA	TGAGCCAGGT	1680
		GCACCCGTAG					1740
		TOGAGGCTGC					1800
20		TOCTGTTTCC					1860
20 .		GTGACAATAA					1920
		TACCTCAAAG					1980
	TATTGCTACA	AAGTGAGTCA	CACAAATTGT	TTTGTTTCCT	TGTGAATATG	AAGTTATATT	2040
		GATGGCTCAT					2100
0.0		CCAGGAATTG					2160
25		AGCTATGTTT					2220
		TTTAAAACTC					2280
		GAGGCCAAGA					2340
		CAAAA CACGT				agaaagaaaa	2400
30	AGAAGAAAAA	CTACTTGCTG	CCCTTACTTG	AAGCTCAATT	ATTTAAAAC		
	Sec ID NO:	16 DNA sec	aence				

Nucleic Acid Accession #: CAT cluster

WC02098558 [file ///E:/WC02098558.cpc]

	1	11	21	31	41	51	
35	1	1	1	1	1	1	
	CTTTTTTTT	TTTTTTTTT	TAGTAGAGAC	AGGGTTTCAC	CATGTTAGCC	AGGATGGTCT	60
	CGATCTCCTG	ACCTCATGAT	CTTCCTGCTT	TGGCCTCCCA	AAGTGCTGCG	ATTACAGGCG	120
		CACCCAGCCC					180
	TCCAGATATA	GGCCCATCAT	AGACATCACA	CAAGCGTGTA	CTTCATAATC	CTGGTGAATA	240
40	CAGAAGTTTC	CTGGACTCCT	TGATGAGCTA	CTGCTTTCGC	TCCTATATCA	GTGTTTTCAG	300
	CIGATGICAT	TIGIGATIGI	GTTTCTGACT	TTCTGTAGGC	AGAAAAAAAC	TTTCATTTTT	360
	TTTTTTGCTTA	CATGCA CATA	AATGTAAGCG	CTAATTCTTA	TATTAAACTG	TTTATTTCTA	420
	TAATACTTAA	TIGGCIGITI	TCCTGGCTGA	ACCARACCRA	GAGCATAAGG	AATGATAACC	480
	TTCAAAACTG	ATTRAATTAG	AGATCAATAA	ATGGAGCTGT	TITAATTCTA	TTATTCTTCT	540
45	TTCATAGATT	AAATAGAAAA	TTTTT				

Seq ID NO: 17 DNA sequence Nucleic Acid Accession #: CAT cluster

50		11	21	31	41	51	
50	i	1	î [*]	î*	T.	Ĭ	
	GGCACGAGAA	GACGCCACAT	CCCCTATTAT	AGAAGAGCTA	ATAAATTTCC	ATGATCACAC	60
	ACTARTART	GITTTCCTAA	TTAGCTCCTT	AGTOCTOTAT	ATCATCTCGC	TAATATTAAC	120
		ACACATACAA					180
55		GTAATCCTTA					240
		AACAACCCCC					300
		ACTGACTATG					360
		GGTGAACTAC					420
60		CGTATATTAA					480
60		AAAACTGATG					540
		TTCTATGGCC			TACCATAGCT	TTTTGCCATT	600
	GTCCTAGAAT	GGGTCCCTAA	AATATTTCGG	NACTGGTCTG			

65 Seq ID NO: 18 DNA sequence Nucleic Acid Accession #: CAT cluster

	HUCZONO HO						
	1	11	21	31	41	51	
	1	1	1	1	1	1	
	GTGTACATCA	GAGCAAAAAT	ACAGAGTATT	TATTCATTTC	TTCCCACTAG	AGGGACACAC	60
70	TGTTCTTGGA	CAGACAAATG	AATCATCAGT	TGTCAGGAGT	TGCCTTTGGA	GAATGATCAA	120
		TTCAGGGGTT					180
		TTCCTGCTCC					240
		TTTCTCGTAG					300
		ATGCTTGTAA					360
75	CAAGCTCGGC	TTCACCANTA	AATATGTTCA	CCAGTGTTAT	GCCAATTATA	ACTGGGATCC	420
		AAGGTAGAAT					480
		AAACAGTCTC					540
	CGGAAANTCC	GCGTGAGAAA	ACTTCCGACT	CCGAGTCTAG	GACCAGCGCG	GCGGCAAGAC	600
	CACGCTGTCA	GCGCGGAGAC	CGAANCCGCT	GCAGCAGCTC	ATGGCCGCCA	TGG	

Seq ID NO: 19 DNA sequence Nucleic Acid Accession #: CAT cluster

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	1	11	21	31	41	51	
	TAGTCCAGTN	ARTTACTTTA	ATTICGCTTT	TOTATAATAC	TEGTATTOCA	TAGAAGAAAA	60
5	TCTTTTTTTA	ATATTCTATA	CTACTACATC	CGACACCAGA	TGACTAAAGT	TTGCAATGGT	120
3						ATTCATTTCA ATATAATTAC	180 240
	AACAGAATGA	AGGATGAGGT	ACAACATACA	TTTTTTGGCAA	TTTACTATTA	AGGGCCATAA	360
10	TCATTTTAGG	GGCGCTTAGG	GCCCATATAT	ATATATATAT	ATTTTTTGGAC	A	
10	Seq ID NO:	20 DNA segr	ience				
	Nucleic Ac:	id Accession	ı ∦: U92072				
	Coaing sequ	sence: 351.	.3701				
15	1	11	21	31	41	51	
	0000000000	maccomorco	l crossome	l .	1	TGCGGGGGTG	60
	CGGGTCATGG	ATGCGGCGGC	AGCGGCGCGG	GACGGCGGGA	GCCCGGCCGC	GACCAGGTGA	120
20	GGAGGCGGCG	TCCGGCGCCA	CTGCAGCCGC	AGCGGCCTCG	GAGGAAGAGG	GCTCGCCGCC	180
20	GCGCGCCCGC	CCGCCGTCGC	GCCGCCTCTA	GTTGGGATTA	TCTTCTGCTC	CCCGCTGCTT	240 300
	GGTGCCTCTG	CTACCTGGGC	CTCGTAGCTG	GGAGACCCTT	GGGCGAGACC	ATGAGGAAAT	360
	TCAACATCAG	GAAGGTGCTG	GACGGCCTGA	CCGCAGGCTC	GTCCTCGGCC	TOGCAACAGC	420
25	AGCAACAGCA	GCAGCACCCG	CCTGGGAACC	GCGAGCCCGA	GATCCAGGAG	ACCCTCAGCC	480 540
	TEGCCTTTGA	TOCCGTTCAG	AAGATCCTGG	CGGTAGGAAC	CCAGACTGGT	GCTTTAAGGC	600
	TCTTTGGTCG	TCCAGGGGTG	GAATGTTATT	GCCAGCACGA	CAGCGGAGCG	GCAGTGATTC GACACCTTAC	660
	ACTOCAGTT	TTTACTTCAG	BARAGGCCC	CTGTGCTACA	TTCACTCAGA	TTTTGCAGAG	720 780
30	AAAGGGTTAC	ATTTTGCCAT	CTGCCTTTCC	AGAGTAAGTG	GCTCTATGTG	GGCACGGAAC	840
	GAGGTAATAT	ACATATTGTC	AATGTGGAGT	CCTTCACACT	CTCAGGCTAC	GTCATTATGT	900 960
	ATAATCCCAT	GGACGAGGG	AAGCTTCTGA	TIGGCTITGA	ATCTGGAACA	CATATAAGTG GTAGTCTTAT	1020
25	OGGACCTTAA	GTCAAAGAAG	GCTGACTACA	GATACACTTA	CGACGAGGCT	ATTCACTCTG	1080
35	TGGCTTGGCA	TCATGAAGGA	AAACAGTTTA	TTTGCAGTCA	TTCTGATGGT	ACATTGACCA GGAAAACAGT	1140
	TARAGGATGG	GAAGAAACCC	GAGCCGTGCA	AGCCTATCCT	CAAGGTYGGAG	TTCRAGACRA	1260
	CAAGATCGGG	GGAACCTTTT	ATTATTTTGT	CGGGAGGCTT	ATCATATGAT	ACCGTGGGAA ATGGACTATT	1320
40	GAAGACCTTG	CTTAACAGTG	ATGCATGGGA	AAAGCAOGGC	AGTGCTGGAA	CAGGAGCCGT	1380 1440
	ATGCTGTGGT	TGTTCTCCTG	GAGAAGGATT	TAGTGCTGAT	AGACCTGGCA	CAGAATGGAT	1500
	ACCCTATATT	TGAGAATCCC	TACCCTTTGA	GTATACACGA	STCCCCTSTT	ACATGTTGTG	1560
	AGRAROTTA	AGGTTACAGC	BEBBBGGBBT	GGCCCATCAA	TOGTOCTANT	GGAGCTAGAC TGGGGCTTGG	1620 1680
45	GTGCTCAAAG	TTACCCAGAA	ATARTTATTA	CAGGGCATGC	TGATGGCTCA	ATTAAATTCT	1740
	GGGATGCTTC	TGCAATAACT	CTACAAGTAC	TGTATAAATT	AAAAACATCT	AAAGTATTTG GATCCATATG	1800 1860
	CCATTCAGAT	CATCTCCTGG	TGCCCAGAGA	GCAGAATGCT	GTGCATAGCC	GGAGTGTCGG	1920
50	CTCATGTCAT	CATTTATAGA	TTCAGCAAGC	AGGAAGTGGT	TACAGAAGTC	GGAGTGTCGG ATCCCGATGC	1980
30	TTGAAGTCCG	CACTCCCCTRG	GAAATAAATG	ATGTGGAAAC	CATCOCCCCT	GAGCAGCCAC	2040
	COTCTACCAG	CAGCAGCTCA	TOGGACGGGC	AATADAGOTT.	TOTACYGTOT	TTABABACTTA	2160
	ARARCTCACC	ACTTAAACAG	TCTCCCGGCT CAGCAGATCA	ATCAAACAGA	GCTAGTCATC	CACTIGGIGI	2220
55	TOOTGOTTET	CGGCAACTCC	AATGGCATTG	CAATGGTTGA	CTACCTCCAG	AAAGCAGTGC	
	TGCTCAACCT	CAGCACCATT	GRACTATACG	GCTCAAATGA	TCCTTATCGG	AGAGAACCGA	2400
	GGTCGCCCCG	CAAATCTCGA	CAGCCTTCAG	GAGCGGGCCT	GTGTGATATT	ACCGAAGGAA AGGAAATTAA	2460 2520
	GCTTGCCAAC	TGATCTAAAG	CCTGATTTAG	ATGTGAAAGA	CAATTCCTTC	AGCAGATCTC	2580
60	GGAGTTCAAG	TGTGACCAGC	ATTGACAAAG	AGTCCC3GGA	AGCCATTTCT		2640
	CCACAGTGGG	PACTROCTTT	AAGGCAGACT GTChTChCGC	TGAATCTCCC	CCCGTGCCTG	TGGGTGGGAA GAGCAGAGAC	2700 2760
	TGCTTCAGCC	AGTGATTGTG	TCTCCAAGCG	GTACTATATT	GAGGTTAAAA	GGTGCGATCT	2820
65	TGAGAATGGC	ATTTCTGGAT	GCCGCGGGCT	GCTTAATGCC	ACCTGCATAC	GAACCCTGGA	2880
05	TOTCAGTGTC	CCCCTCCTCT	TCTYAGGAAA	TTAGTGABAA	CCACTACACA	CGGCGACCTG	2940 3000
	CTGAAAAGCA	AGCARAGGTC	ATCTCACTGC	CARCCCAGAR	CTGTGCATAC	AAGCAGAACA	3060
	TCACTGAGAC	GTCCTTCGTG	CTCCGTGGAG	ACATTGTCGC	CCTGACTAAC	AGTGTCTGCC TTGAGGCCTC	3120 3180
70	TGCTGGATGT	CTACTACCTG	CCCCTTACCA	ACATGCGGAT	AGCCAGGACA	TTCTGCTTCG	3240
	CCANCAGTGG	GCAAGCCTTA	TACCTTGTTT	CACCTACCGA	AATCCAGAGA	CTCACCTACA	3300
	GTCAGGAGAC	GTGTGAAAAC	CTTCAGGAGA GGGTTCTTCA	TGCTTGGTGA	GCTCTTCAC3	CCTGTAGAAA	3360 3420
	TTGATAGAGA	AGAACTGTTT	GGAGAGTCAT	CCTCGGGAAA	GGCGTCAAGG	AGCCTTGCAC	3480
75	AGCACATCCC	GGGTCCTGGC	GGGATCGAAG	GTGTGAAGGG	AGCCGCGTCG	GGAGTGGTGG	3540
	GAGAACTGGC ABGAGAGGAC	TGCAGCCATC	ATGTCCAGTG	CAGACTOCTT	ACAGAAGCTC TTCCAAAC2T	AGCGACTTGG GCTCATGAGA	3600 3660
	TGATGCTGAA	ATACAAAGAT	AAGAAGTGGT	ACCAGTTCTG	ACAAGTAGCA	CTCAGTAAGT	3720
80	CCAGCTTCAA	CCAGAAGGAA	AAAGACGTTT ACACTGCTGA	CCTTGTTGAG	GTCACTGATG	TATTTGGGAA	3780
30	MUATAACATA	MANUGUATGC	ACACTECTEA	CHOCOTCITT	CCCAGCACAA	LUATECACTT	

Seq ID NO: 21 Protein sequence Protein Accession #: AAD04756

	1	11	21	31	41	51.	
	1	1	1	1	1	1	
_	MRKFNIRKVL	DGLTAGSSSA	SQQQQQQQHP	PGNREPBIQE	TLQSEHFQLC	KTVRHGFPYQ	60
5	PSALAPDPVQ	KILAVGTQTG	ALRLPGRPGV	BCYCQHDSGA	AVIOLOPLIN	BGALVSALAD	120
		KRPAVLHSLK					180
		SSKSHPGPVV					240
		KQFICSHSDG					300
10		IILSGGLSYD					360
10		EKDLVLIDLA					420
		KKEWPINGGN					480
	KVFEKSRNKD	DRONTDIVDE	DPYAIQIISW	CPESRMLCIA	GVSAHVIIYR	FSKQEVVTEV	540
	IPMLEVRLLY	EINDVETPEG	EQPPPLSTPV	GSSTSQPIPP	QSHPSTSSSS	SDGLRDNVPC	600
	LKVKNSPLKQ	SPGYQTELVI	QLVNVGGEPP	QQITSLALNS	SYGLVVFGNS	MGIAMADAFÓ.	660
15	KAVLLNLSTI	ELYGSNDPYR	REPRSPRKSR	QPSGAGLCDI	TEGTVVPEDR	CKSPTSAKMS	720
	RKLSLPTDLK	PDLDVKDNSF	SRSRSSSVTS	IDKESREALS	ALHFCETFTR	KADSSPSPCL	780
	WVGTTVGTAF	VITLNLPLGP	BORLLOPVIV	SPSGTILRLK	GAILEMAFLD	AAGCLMPPAY	840
		EKDEKEKTKK					900
		LRGDIVALSN					960
20	PCFANSGOAL	YLVSPTEIOR	LTYSOFTCEN	LORMLGELFT	PVETPEAPNR	GFFKGLFGGG	1020
	AOSLDREELF	GESSSGKASR	SLAQHIPGPG	GIEGVKGAAS	GVVGELARAR	LALDERGOKL	1080
	SDLEERTAAM	MSSADSFSKH	AHEMMLKYKD	KKWYQF			

25 Seq ID NO: 22 DNA sequence Nucleic Acid Accession #: CAT cluster

	1	11	21	31	41	51	
	1		1	I	1	1	
20		TGAACCGTGG					60
30	GCCCCGGCAA	AGCCTGGCTC	GTTCACAGCT	CTCTCGCACC	TCCTGGAGCT	TCAGCTTCTT	120
	CCGTTGCAGA	GAAGCTTTAT	GGGCCAATTC	GTTCGGCATC	CCGGGGGGCAG	GTGCGCGGTG	180
	CGCGGGGAAG	AAGAGGATTT	GACTGCGGTT	CTCCACCCC	GGCGCCCAAC	CTCCACCCCG	240
	GTGCGCGCGC	TCTTCCAGGC	TCCTGCTGGT	CCCACTTGCC	AGGAGTTAGG	TCTCAGGTCA	300
	GCCTGAGCTC	CTGAGACGCC	CAGGCCCGGA	AAGACACGTA	GGGGAAACCA	TCTGCTCACT	360
35		CCGGAAGGGA					420
	GCCTTGAGAT	AAGCAATGCT	GAAGCACTIG	CAGCTCACCT	ATTACCATAA	ACTGACTGAG	480
	CCCTCCCTAC	ACAAGCCGTA	ACTACTGCTT	TGATTGGACA	AGAGACTGAT	TTCAGTAGTT	540
	TTCTCTTGAT	AAGAGACCAC	TGGCCGTGGG	CGGGTTCTGG	ACAGTTTACA	GAAGCTATGC	600
	ACTTGATTGC	CTTTGTGTCC	CTGCTTCACC	TTTTGAAGCA	TAGGGCCTAA	TTATAATGTA	660
40		GTCTCCACCC					720
	AGCATGCATG	CAGCAGGATC	CCTTCACAAA	TATTCAGAGC	TCCCCCTATT	CCCTGTTGAA	780
	TATGTATATG	TGGCCAGCCA	GATCAACGTA	AATCACTATT	CGCCCTCCCC	TCCCTGGAAA	840
	CCTACTTTTC	GGGTTTCAGC	AGGAAGCTAT	GCCTCCCAGG	CTTGTCGAAG	AGGGCCCATT	900
	TTCGGGCTTG	ATAACCCCTT	TATAAAAAAA	TAAAATCTCC	TTTCTAAATT	TAAAATACAA	960
45	CCACACCACC	GGCCCGCAAC	TATTGGGGGG	GAAAAAGAAT	GAAGACACAC	GGTACATAGT	1020
	TTCATGCACA	TTGTTAAGGA	GACAGGTGCC	CCCAAGCAGG	CGGACATCAC	GCAGTACGCA	1080
	GCTTGAGCAT	GCCGAAGACG	CGAGCGACTC	ATAGAACACG	ACGACGCTCG	CAAGGCACTA	1140
	AGCATAGCTA	CTACCACTOG	TCGAAGAGTC	ATACACAGAT	TTCTATTGGC	GA	

50 Seq ID NO: 23 DNA sequence Nucleic Acid Accession 8: CAT cluster

65
Seq ID NO: 24 DNA sequence
Nucleic Acid Accession #: NM_000044.1
Coding sequence: 1115..3874

70 COAGATCCCS GGOAGCCAGC TROCTGGOAG AGCOGGACGS TCCSGAGGAA GCCCACAGGC AGAGGAGGCS ACAGAGGGAA AAAGGGCCSA GCTAGCCGCT CCAGTGCTST ACAGGAGCCG 120 ANAGORAGO ANAGORAGORAGO ANAGORAGO ANAGORAGO ANAGORAGO ANAGORAGO ANAGORAGO ANAGORAGOR 75 240 200 360 420 GCCCCCCCC CCCGTCGGC CCAGCGCTGC CAGCCCGAGT TTGCAGAGAG GTAACTCCCT 480 80 TIGGCTOCGA GCGGGCGAGC TAGCTGCACA TIGCAAAGAA GGCTCTTAGG AGCCAGGCGA 540 CTGGGGAGCG GCTTCAGCAC TGCAGCCACG ACCCGCCTGG TTAGAATTCC GGCGGAGAGA 600 ACCCTOTOT TROCCCOACT CTCTCTCCAC CTCCTCCTGC CTTCCCCACC CCGAGTGCGG 660 AGCAGAGATC AAAAGATGAA AAGGCAGTCA GGTCTTCAGT AGCCAAAAAA CAAAACAAAC 720

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ARARACAARA RAGCCGRART ARANGAARA GATRATRACT CAGTTCTTAT TTGCACCTAC 780 TICAGTGGAC ACTGAATTIG GAAGGTGGAG GATITIGTET TITTCTTTTA AGATCTGGGC 840 ATCTTTGAR TCTACCCTTC ARGTATTARG AGRICAGRITG TGROCCTAGIC AGGGCAGATC TTSTCCACCG TGTGTCTTCT TCTGCACGAG ACTTTGAGGC TGTCAGAGCG CTTTTTGGT
GGTTGCTCCC GCAAGTTTCC TTCTCTGGAG CTTCCCGCAG GTGGCGAGCT AGCTGCAGCG 5 ACTACCGCAT CATCACAGCC TGTTGAACTC TTCTGAGCAA GAGAAGGGGA GGCGGGGTAA 1080 GGGAAGTAGG TGGAAGATTC AGCCAAGCTC AAGGATGGAA GTGCAGTTAG GGCTGGGAAG 1140 GGTCTACCCT CGCCCGCCGT CCAAGACCTA CCGAGGAGCT TTCCAGAATC TGTTCCAGAG 1200 CGTGCGCGAA GTGATCCAGA ACCCGGGCCC CAGGCACCCA GAGGCCGCGA GCGCAGCACC 1260 10 TCCCGGCGCC AGTTTGCTGC TGCTGCAGCA GCAGCAGCAG CAGCAGCAGC AGCAGCAGCA GCASCAGCAS CAGCAGCAGC AGCASCAAGA GACTAGCCCC AGGCAGCAGC AGCAGCAGCA GGGTGAGGAT GGTTCTCCCC AGCCCATCG TAGAGGCCCC ACAGGCTACC TGGTCCTGGA 1200 1440 TGAGGAACAG CAACCTTCAC AGCCGCAGTC GGCCCTGGAG TGCCACCCCG AGAGAGGTTG 1500 CGTCCCAGAG CCTGGAGCCG CCGTGGCCGC CAGCAAGGGG CTGCCGCAGC AGCTGCCAGC 15 ACCTOCGGAC GAGGATGACT CAGCTGCCCC ATCCACGTTG TCCCTGCTGG GCCCCACTTT 1626 CCCCGGCTTA AGCAGCTGCT CCGCTGACCT TAAAGACATC CTGAGCGAGG CCAGCACCAT 1680 GCAACTCCTT CAGCAACAGC AGCAGGAAGC AGTATCCGAA GGCAGCAGCA GCGGGAGAGC 1740 GAGGGAGGCC TCGGGGGCTC CCACTTCCTC CAAGGACAAT TACTTAGGGG GCACTTCGAC 1800 CATTTCTGAC AACGCCAAGG AGTTGTGTAA GGCAGTGTCG GTGTCCATGG GCCTGGGTGT 20 GGAGGGTTG GAGCATCTGA GTCCAGGGGA ACAGCTTCGG GGGGATTGCA TGTACGCCCC ACTTTTGGGA GTTCCACCCG CTGTGCGTCC CACTCCTTGT GCCCCATTGG CCGAATGCAA 1920 1980 AGSTTCTCTG CTAGACGACA GCGCAGGCAA GAGCACTGAA GATACTGCTG ASTATTCCCC TTTCAAGGGA GGTTACACCA AAGGGCTAGA AGGCGAGAGC CTAGGCTGCT CTGGCAGCGC 2040 2100 TOCAGCAGGG AGCTCCOGGA CACTTGAACT GCCGTCTACC CTGTCTCTCT ACAAGTCCGG 2.5 AGCACTGGAC GAGGCAGCTG CGTACCAGAG TCGCGACTAC TACAACTTTC CACTGGCTCT GOCCGGACCG CCGCCCCTC CGCCGCCTCC CCATCCCCAC GCTCGCATCA AGCTGGAGAA 2200 COCGCTGGAC TACGGCAGCG CCTGGGCGGC TGCGGCGGCG CAGTGCCGCT ATGGGGACCT 2340 GGCGAGCCTG CATGGCGCGG GTGCAGCGGG ACCCGGTTCT GGGTCACCCT CAGCCGCCGC 2400 TTCCTCATCC TGGCACACTC TCTTCACAGC CGAAGAAGGC CAGTTGTATG GACCGTGTGG 30 CEGCGGCGGC GAGGCGGGAG CTGTAGCCCC CTACGGCTAC ACTCEGCCCC CTCAGGGGCT 2500 GGCGGGCCAG GAAAGCGACT TCACCGCACC TGATGTGTGG TACCCTGGCG GCATGGTGAG 2640 CAGAGTUCCC TATCCCAGTC CCACTTGTGT CAAAAGCGAA ATGGGCCCCT GGATGGATAG 2700 CTACTCCGGA CCTTACGGGG ACATGCGTTT GGAGACTGCC AGGGACCATG TTTTGCCCAT 2760 35 TGACTATTAC TTTCCACCCC AGAAGACCTG CCTGATCTGT GGAGATGAAG CTTCTGGGTG TCACTATGGA GCTCTCACAT GTGGAAGCTG CAAGGTCTTC TTCAAAAGAG CCGCTGAAGG 2880 GARACAGARG TACCTGTGGG CCAGCAGAA TGATTGCACT ATTGATAAAT TCCGAAGGRA AAATTGTCCA TCTTGTCGTC TTCGGAAATG TTATGAAGCA GGGATGACTC TGGGAGCCCG 2940 3000 GAAGCTGAAG AAACTTGGTA ATCTGAAACT ACAGGAGGAA GGAGAGGCTT CCAGCACCAC 3060 40 CASCCCCAC GAGGAGACA CCCAGAGC GACAGTOTCA CACATTOAAG GCTATGAAG TCAGCCCAT TITCTGAATG TCCTGGAAGC CATTGAGCA GGTGTAGTGT TTGCTGGAGC CGACAACAAC CAGCCCGACT CCTTGCAGC CTTGTTCTCT AGCTCAATG AACTGGAGA 3120 2240 GAGACAGCTT GTACACGTGG TCAAGTGGGC CAAGGCCTTG CCTGGCTTCC GCAACTTACA 3300 CGTGGACGAC CAGATGGCTG TCATTCAGTA CTCCTGGATG GGGCTCATGG TGTTTGCCAT 3360 45 GGGCTGGCGA TCCTTCACCA ATGTCAACTC CAGGATGCTC TACTTCGCCC CTGATCTGGT 3420 TTTCAATGAG TACCGCATGC ACAAGTCCCG GATGTACAGC CAGTGTGTCC GAATGAGGCA 3480 CONCENTRAL GROUPERS GROUPERS CACCOCCOCCA GRAPHICO PARTICIPAL ACCOCCACA GRAPHICA GRAP 3540 ACTECTACTC TTCAGCATTA TTCCAGTEGA TEGGCTEGAA AATCAAAAAT TCTTTGATGA ACTTCGAATG AACTACATCA AGGAACTCGA TCGTATCATT GCATGCAAAA GAAAAAATCC 3.600 3660 50 CACATCOTEC TCAAGACGCT TCTACCAGCT CACCAAGCTC CTGGACTCCG TGCAGCCTAT 3720 TGCGAGAGAG CTGCATCAGT TCACTTTTGA CCTGCTAATC AAGTCACACA TGGTGAGCGT GGACTTTCCG GAAATGATGG CAGAGATCAT CTCTGTGCAA GTGCCCAAGA TCCTTTCTGG 3780 3840 GARAGTCARG CCCATCTATT TCCACACCCA GTGRAGCATT GGRARCCCTA TTTCCCCCACC 3900 CORGOTORIG COCCOTTICA GRISTOTTOT GOCTOTTATA ACTOTOCACT ACTOCOTOTOC 3960 55 AGTGCCTTGG GGAATTTCCT CTATTGATGT ACACTCTGTC ATGAACATGT TCCTGAATTC 4020 4080 AACCCTCCCA TGGCACCTTC AGACTTTGCT TCCCATTGTG GCTCCTATCT GTGTTTTGAA 4140 TGGTGTTGTA TGCCTTTAAA TCTGTGATGA TCCTCATATG GCCCAGTGTC AAGTTGTGCT 4200 TOTTTACAGC ACTACTOTO GCCAGCCACA CAAACOTTTA CTTATCTTAT GCCACGGGAA 4260 60 Sec ID NO: 25 Protein semience Protein Accession 8: NP 000035.1 65 MEVOLGLGRV YPRPPSKTYR GAPONLPOSV REVIONPGPR HPEAASAAPP GASLLLLOOO 60 QQQQQQQQQQ QQQQQQQQET SPRQQQQQQG EDGSPQAHRR GPTGYLVLDE EQQPSQPQSA 120 70 LECHPERGCV PEPGAAVAAS KGLPQQLPAP PDEDDSAAPS TLSLLGPTFP GLSSCSADLK DILSEASTMQ LLQQQQQEAV SEGSSSGRAR EASGAPTSSK DNYLGGTSTI SDNAKELCKA VSVSMGLGVE ALEHLSPGEQ LRGDCMYAPL LGVPPAVRFT PCAPLAECKG SLLDDSAGKS 300 360

TECTAEYSPF KOGYTKGLEG ESLGCSUSAA AGSSOTLELP STLSLYKSGA LDEAAAYOSE DYYNFFLALA GPPPPPPPP PHARIKLENF LDYGSANAAA AAOCRYGDIA SLHCAGAAGF 420 GYTRPPOGLA GOESDFTAFD WWYFGGMVSR VPYPSPTCVK SENGPWNDSY SGPYGDMRLE 540 TARDHVLPID YYPPPQKTCL ICGDRASGCH YGALTCGSCK VPFKRAABGK QKYLCASRND 600 CTIDEPREEN CPSCELEKCY EAGNILGARK LKKLGHLKLO EBGEASSTIS PIEETTOKLT 660 VSHIEGYECO PIPLNVLEAI ERGVVCAGHD NNOPDSPAAL LSSLNELGER OLVHVVKWAK 720 ALPGFRNLHV DDQMAVIQYS WMGLMVFAMG WRSFTNVNSR MLYFAFDLVF NEYRMHKSRM YSQCVEMBEL SQEFGWLQIT POEFLCMKAL LLFSTIPVDG LMNQKFFDEL RMNYIKELDR IIACKRKNPT SCSRFFYQLT KLLDSVQPIA RELHQFTFDL LIKSHMVSVD FPEMMAETIS 900 VOVPKILAGE VEPIEFHTO

75

Seq ID NO: 26 DNA sequence Nucleic Acid Accession #: CAT cluster

5	1	11	21	31	41	51	
	1	1	1	1	1	1	
	AGCATTATCC	ATGGCCAGTG	ATTGATGGAC	TTGTTCAGGT	CCTATGCAGA	GTGCTTCATA	60
10	TATCTCATCT	CANTCCTCTA	AATAACCATG	AAAGTTGATG	ATTATCTCAT	GGTACAGATG	120
	GGAGGCTAAG	AGTGTTTAAT	TTTCCCCAAG	TTCCAGTGCT	ACTAACTGTT	CHINNINININI	180
10	NNTGAACCTG	TGTTAATGGT	GTTTCTAGTC	GATGCTGTTA	TCTGTTGCAC	CACATTTIGA	240
	ATAATCTTGG	ACTITCAGAG	TATGAAGGAC	GATTAAATAT	AACCCTTTGG	TATAAATGTT	300
	CTCTCTCTCG	CTCCTCTGTA	ACAATTGGAG	AAACAGAGTT	CTAACAATAT	TANANTCAGC	360
	CATAGACAGA	GAGTAGTGAG	AAATATACTT	TTTTTAATAC	AGAAGGTTCC	CTGAAGTACT	420
	TTTAGTATTA	TTCTAAATTA	AGCANTANCO	ANTGAACAAT	TTTGGTCATA	AGCAGTTTCT	480
15	CTCCAGAAAA	AAAAAAAAA	AGTCGAC				

Seq ID NO: 27 DNA sequence Nucleic Acid Accession #: NM_006551.2

20	Nucleic Acid Accession #: NM_006551.2 Coding sequence: 64336								
-0	1	11	21	31	41	51			
	AATTCTAGAA	GTCCAAATCA	CTCATTGTTT	GTGANAGCTG	AGCTCACAGC	AAAACAAGCC			
25		TGTCGGTGTG							
23		AGTTAAGTCT							
		AGAGATGCAC							
		AAATATTGAA							
20		TTCAATGACA		CACTGCAGAA	TGTAAAGGTT	TCAACGTCTT			
30	GCTTTAATAA	ATCACTTGCT	CTAC						

Seq ID NO: 28 Protein sequence Protein Accession #: NP_006542.1

35	1	11	21	31	41	51	
	1	1	1	1	1	1	
	WKTSACTTTA	TLALCCYQAN	AEFCPALVSE	LLDFFFISEP	LFKLSLAKFD	APPEAVAAKL	60
	GUYRCTTOMS	LOXBSLIARY	LAKITHERCSY				

40 Seq ID NO: 29 DNA sequence Nucleic Acid Accession 8: NM_002645.1 Coding sequence: 1..5061

		TATTTAGCAA					60
		AAGATGTGGA					120
	AAACTGCAAA	AGGATAGACA	AGTGACTGAC	AATCAGAGAG	GCTTTGAGTT	GTCAAGCAGC	180
	ACCAGAAAAA	AAGCACAGGT	TTATAACAAG	CAGGATTATG	ATCTCATGGT	GTTTCCTGAA	240
50	TCAGATTCCC	AAAAAAGAGC	ATTAGATATT	GATGTAGAAA	AGCTCACCCA	AGCTGAACTT	300
	GAGAAACTAT	TGCTGGATGA	CAGTTTCGAG	ACTAAAAAAA	CACCTGTATT	ACCAGTTACT	360
	CCTATTCTGA	GCCCTTCCTT	TTCAGCACAG	CICIATITIA	GACCTACTAT	TCAGAGAGGA	420
	CAGTGGCCAC	CTGGATTACC	TGGGCCTTCC	ACTIATOCTI	TACCTTCTAT	TTATCCTTCT	480
		AACAGGCTGC					540
55		CTATATATTT					600
		CACCCTTTCA					660
		CAAAACTATT					720
		CTGATTTGGA					780
		ATATCAGTAA					840
60		TGGAGGTATT					900
		GGGATGCTGT					960
		ATGGAAAATC					1020
		CTCAGCTTGC					1080
		TGCCAACTGG					1140
65		TTTGTCGATC					1200
		CAGGCTATTT					1260
		TGAAGGTCTC					1320
		GTTCTACTGT					1380
		AAGTAGATGT					1440
70		ATCATTGCCT					1500
		GACTACAACT					1560
		ATGAAACACC					1620
		CCATGACGAG					1680
70		CTCTTCAAAT					1740
75		TCTGTAGTGC					1800
		AGAGAGCAGT					1860
		AAGACACTAG					1920
		GCATAAACCA					1980
00		GGAGTCCTAC					2040
80		AGCAGCTCCA					2100
		ATGAAAAATA					2160
		TTCAATCAAA					2220
	TGGGATGAAC	TANTCATTTT	TCCTATCCAG	ATATCACAAT	TGCCATTAGA	ATCAGTTCTT	2280

CACCTTACTC TTTTTGGAAT TTTAAATCMG AGCAGTGGAA GTTCCCCTGA TTCTAATAAG 2340 Chicarana december were contained the contract of the contract 2400 TTTTFACAT GTGGAACTAA ACTTCTATAT CTTTGGACTT CATCACATAC AAATTCTGTT 2460 CCTGGAACAG TTACCAAAAA AGGATATGTC ATGGAAAGAA TAGTGCTACA GGTTGATTTT 2520 5 CCTTCTCCTG CATTTGATAT TATTTATACA ACTCCTCAAG TTGACAGAAG CATTATACAG CARCATARCT TAGRARCACT AGAGRATGRY ATRARAGOGA RACITOTIGA TATTOTICAT 2640 ARRESTORY CASTROGRACT TRUTARRESS GREENSCOTT TRUTATORIS GREENSCOTAT 2700 TATTGCTTCA AACACCCAAA TTGTCTTCCT AAAATATTAG CAAGCGCCCC AAACTGGAAA 2760 TOGGGTAATC TTGCCAAAAC TTACTCATTG CTTCACCAGT GGCCTGCATT GTACCCACTA 2820 10 AFTGCATTGG AACTTCTTGA TTCANAATTT GCTGATCAGG AAGTAMGATC CCTAGCTGTG ACCTGGATTG AGGCCATTAG TGATGATGAG CTAACCAGATC TTCTTCCAG GTTTGTACAA GCTTTGAAAT ATGAAATTTTA GTTGAATAGT TCATTAGTGC AATTCCTTTT GTCCAGGGCA 2940 3000 TIGGGAAATA TCCAGATAGC ACACAATTTA TATTGGCTTC TCAAAGATGC CCTGCATGAT 3060 GTACAGTTTA GTACCCGATA CGAACATGTT TTOOGTGCTC TCCTGTCAGT AGGAGGAAAA 15 CGACTTAGAG AAGAACTTCT AAAACAGACG AAACTTGTAC AGCTTTTAGG AGGAGTAGCA 3180 GARARAGTAA GGCAGGCTAG TGGATCAGCC AGACAGGTTG TTCTCCARAG AAGTATGGAA 3240 CCAGTACAGT COTTTTTTCA GAAAATAAA TGCCGTCTCC CTCTCAAGCC AAGTCTAGTG 3300 GCAAAAGAAT TAAATATTAA GTCGTGTTCC TTCTTCAGTT CTAATGCTGT CCCCCTAAAA 3360 GTCACAATGG TGAATGCTGA CCCTCTGGGA GAAGAAATTA ATGTCATGTT TAAGGTTGGT 3420 20 GARGATOTTO GGCARGATAT GTTAGOTTTA CAGATGATAA AGATTATGGA TAAGATOTGG CTTARAGRAG GACTAGATCT GAGGATGGTA ATTTTCARAT GTCTCTCARC TGGCAGAGAT 3540 CGAGGCATGG TGGAGCTGGT TCCTGCTTCC GATACCCTCA GGAAAATCCA AGTGGAATAT 3600 GGTGTGACAG GATCCTTTAA AGATAAACCA CTTGCAGAGT GGCTAAGGAA ATACAATCCC 3660 POTENTIAL AND THE TOTAL AND COUNTY OF THE STREET AND COUNTY OF THE STREET, THE 3720 2.5 GTAGCCACCT ATGTTTTAGG CATCTGTGAT CGACACAATG ACAATATAAT GCTTCGAAGC 3780 ACGGGACACA TGTTTCACAT TGACTTTGGA AAGTTTTTGG GACATGCACA GATGTTTGGC AGCTTCAAAA GGGATCGGGC TCCTTTTGTG CTGACCTCTG ATATGGCATA TGTCATTAAT 3900 GGGGGTGARA AGCCCACCAT TOSTITITCAS TISTITIGIGS ACCICIGCIS TCAGGCCTAC
AACTIGATAA GARAGCAGAC AAACCTITIT CITRACCICC TITCACTGAT GATTCCTTCA 3960 4020 30 GGGTTACCAG AACTTACAAG TATTCAAGAT TTGAAATACG TTAGAGATGC ACTTCAACCC 4080 CAAACTACAG ACGCAGAAGC TACAATTITC TTTACTAGGC TTATTGAATC AAGTTTGGGA AGCATTGCCA CAAAGTTTAA CTTCTTCATT CACAACCTTG CTCAGCTTCG TTTTTCTGGT 4200 CONCENTED ANGANGAGO: CANCENTED STRUCKCOTA ALLCATACHC CONTAGACA 42.60 GATGGTCGAA TCAAGGAAGT CTCTGTTTTT ACATATCATA AGAAATACAA CCCAGATAAA 4320 35 CATTATATT ATGTAGTCCG AATTTTGTGG GAAGGACAGA TTGAACCATC ATTTGTCTTC 4380 CGAACATTG TOGAATTCA GGAACITCAC AATAAGCTCA GTATTATTTT TCCACTTTGG 4440 ARGITACCAG GCTTTCCTAA TAGGATGGTT CTAGGAAGAA CACACATAAA AGATGTAGCA 4500 GCCAAAAGGA AAATTGAGTT AAACAGTTAC TTACAGAGTT TGATGAATGC TTCAACGGAT 4560 GRAGORGAGE GOGLECCENCE STORECTEC TROCECCCTT TACTFOOTGE TGEGALACCT 4620 40 GAAGGGATAG CTAGGTCTGC AGATGCAGGT TCCTTCAGTC CTACTCCAGG CCAAATAGGA 4680 GGAGCTGTGA AATTATCCAT CTCTTACCGA AATGGTACTC TTTTCATCAT GGTGATGCAT ATCARAGATO TIGITACIGA AGATEGAGOT GACCCARATO CATATGICAR RACATACCIA 4800 CTICCAGATA ACCACARARC ATCOMMICST ANANCEARM TITCACGARA RACGAGGRAT CCGACATTCA ATGRATICCT TOTATACAGT GGATATAGCA AAGGARCCT AAGACAGCAG GRACTICAAC TAAGUCTACT CAUTGAGAGA CTCTCGGGGG AAAATITTT CTTCGGGGGA GTAACCCTGC CTTTGAARGA TITCAACTTG AGCARAGAGA CGGTTAAATG GTATCAGCTG 4860 4920 45 4980 ACTOCOGCAA CATACTTOTA A

50 Seq ID NO: 30 Protein sequence Protein Accession #: NP 002636.1

TYTAKT

31 MAGIPSNEGF KECPFSHPEP TRAKDVDKEE ALOMEARALA KLOKDROVTD NORGFELSSS 55 TRKKAOVYNK ODYDLMVFPE SDSOKRALDI DVEKLTOAEL EKLLLDDSFE TKKTPVLPVT 120 PILSPSFSAO LYFRPTIORG OWPPGLPGPS TYALPSIYPS TYSKQAAFON GFNPRMPTFF 180 STEPIYLSLP GOSPYFSYPL TPATPFHPOG SLPIYRPVVS TDMAKLPDKI ASTSEFLKNG KARTDLEITD SKYSNLQVSP KSEDISKFDW LDLDPLSKPK VDWVEVLDHE EEKWVSSLLA 300 KOPWDAVLLE ERSTANCHLE RKVNGKSLSV ATVTRSQSLN IRTTQLAKAQ GHISQKDPNG 360 60 TSSLPTGSSL LQEVEVQNEE MAAFCRSITK LKTKFPYTNH RTNPGYLLSP VTAQRNICGE 420 NASVKYSIDI EGFQLPYTFT CDVSSTVEII IMQALCWVHD DLNQVDVGSY VLKVCGQEEV 480 LONNHOLGSH EHIGNORKWD TEIRLOLLTF SAMCONLART AEDDETPVDL NKHLYGIEKP CKEAMTREPV EELLDSYHRQ VELALQIENQ HRAVDQVIKA VRKICSALDG VETLAITESV KKLKEAVNLP BEKTADVISL PGGEDISESS TRGSINDENP VOVSINGLTA AIVDLIBLHA 660 65 NEGREPTICA OS SKSVKEAN TITEOLOFTI PAAHGISSNW VENYEKYYLI CELSENGKOL 720 FKPIQSKKVG TYKNFFYLIK WDELIFFIQ ISQLPLESVL HLTLFGILNQ SSGSSPDSNK ORKGPEALGK VSLPLCDFRR PLTCGTKLLY LWTSSHTNSV PCTVTKKGYV MERIVLOVDF 840 PSPAFDIIYT TPOVDRSIIO OHNLETLEND IKCKLLDILH KOSSLGLSKE DKAFLWEKRY 900 YCPKHPNCLP KILASAPNWK NGNLAKTYSL LHOWPALYPL IALBLIDSKF ADDEVRSLAV 960 70 THIEAISDDE LTDLLPOPVO ALKYEIYLMS SLWOFLLSRA LCNIQIAHNL YMLLKDALHD 1020 VOFSTRYEHV LGALLSVGGK RLREELLKOT KLVOLLGGVA EKVROASGSA ROVVLORSME 1080 RVOSFFOKNK CRLPLKPSLV AKBLNIKSCS FFSSNAVPLK VINVNADPLG BEINVMFKVG 1200 EDLRODMLAL QMIKIMDKIW LKEGLDLRHV IFKCLSTGRD RONVELVPAS DTLRKIQVEY CUTGSPENCE LARNIERYND SEERVERASE NETYSCAGOC VATYVIGTOD BUNDNIMIES 1260 75 TGHNFHIDFG KFLGHAQMFG SFKRDRAPFV LTSUMAYVIN GGEKPTIRFQ LFVDLCCQAY 1320 NLIRKOTNLF LNLLSLMIPS GLPELTSIGD LKYVRDALOP OTTDAEATIF FTRLIESSLG 1380 SIATKFNFFI HNLAQLRFSG LPSMDEPILS FSPKTYSFRQ DGRIKEVSVF TYHKKYMPDK 1440 HYIYVVRILM EGQIEPSFVF RTFVEFQELH MKLSIIFPLM KLPGFPNRMV LGRTHIKDVA 1500 AKRKIRLNSY LOSLAWASTD VARCOLUCTF PHPLLPDEKA ECTARSADAG SFSPTPGDIG 1560 80 GAVKLSISYR NGTLFIMVMI IKDLVTEDGA DPNPYVKTYL LPDNHKTSKR KTKISRKTRN 1620 PTFNEMLVYS GYSKETLEGE ELOLSVLSAE SLEENFFLGG VILPLEDFNL SKETVKWYGL

15

Seq ID NO: 31 DNA sequence Nucleic Acid Accession #: CAT cluster

5	1 	11 AGACTAAACC	21 ATAGCANGGA	31 	41 - ACTGTATAGC	51 - -	60
10	ACCTCABART TTGGTATTT TATGARAAA GTGATTTGTT AGATGAGCAC AFTTATTTTT	AGACTAGACC ACATTCTGGA CACTGTCAAT AGCTACCTCAC AAGCACTCAC TGACTTTCCC CTTGTATCCA TTTGTTTTTG	ATTTGTAAGG TATGCCTCGT TAGAGCTCAT ATCAATAAAA CATTGAGGAG TAGCTGGGTT	GATGCTTTCG ATTATTTATT GACACATAAT TATTTCAGCT TCTCGATTAC CAAGAGTTCT	TOGACTITTE TATTIGCCAA AGGTATICAC CAACAGGCAC CTCATGTCIC TICITGTITE	TTTTTTTTT AATACGACTG TGAGCATTTG ACTAGGGGCC ACTTCAAACA GTCGGATATA	120 180 240 300 360 420

Seq ID NO: 32 DNA sequence Nucleic Acid Accession #: CAT cluste

	Nucleic Acid Accession #: CAT cluster									
	1	11	21	31	41	51				
20	CAGTCAGATT	TTTTTTTTTCC	TTAACTAAGA	CAAAGTGAAT	AATTCACTGT	GAGCCAAATT	60			
	CITTCITGAT	TCCTCTTTTT	GGAGCAGTCC	ATCTTTATGG	GANANCCAGC	CTAGAATGGT	120			
	GATTTCAGTT	TCAGGTGATT	TCGATAGAAT	TGTATTTGGC	TCAGAAATGA	TAAGACTGGG	180			
	GCCAAGAAAA	ATTTTAAACT	TTTTTTTTTG	TAATCATATT	ACTAGTTTGA	TTTCATATGA	240			
~ -	ACTTCCTTTG	TIGACTITICT	TTGCCATTAA	TTTAAAAGTT	CCAGTATCCT	CARTATITGA	300			
25	TGTCTTATAT	GTACAGAATC	CTTTCCAGCT	GTAAGTCATC	AGCAAGTAAA	AAATTTAGTA	360			
	TGGCAATAGT	TTTCATAAGA	GGTTTTTTAA	AACAGAAAAA	TGTTGACATT	GCCAGCCTCT	420			
						AGGCAAAGAC	480			
	TTTTTCAACA	TCTGAATATT	CTGATTTACA	GAAATTATAA	aaaaaaagt	CGACGCG				
30	Sec ID NO:	33 DMA seco	uence							

5U Seq ID NO: 33 DNA sequence Nucleic Acid Accession #: AK026418.1

	NUCLEIC ACID ACCESSION #: ANDIOGEO.I						
	1	11	21 	31	41	51	
`35	TTTTAAGATG	GAGTTTTCGC	TCTTGTTGCC	CAGGCTGGAG	TGCAGTGGTG	CAATCTTGGC	60
	TCACTGCAAC	CTCTGCCCCC	CGGGTTCAGG	CGATTCTCTC	CTCTCAGTCT	CTCAAGTAAC	120
		GGCACACACC					180
		ATATTGGCCT					240
40		AGCCAGCCAC					300
40		CCAAGAATTG					360
		TTAATATAAC					420
		AAAAGTGGAA					480
		GGTGTCACAT					540
4.5		ACTCCAACTG					600
45		TAGTAATATT					660
		TGTAGCCAAA					720
		TTTAGAACGT					780
		GGTTTTTCAG					840
		AACACTTTGG					900
50		TAATAGAAAT					960
		TTATAGAAGT					1020
		CCCTAAATTT					1080
		ACTGAATTCA					1140
		AGAGCCCTCT					1200
55		ATGGATAATG					1260
		GACTGCAGTA					1320
		TGGTGGGGGA					1380
		AATTAATAAG					1440
		TAGTGAAAGA					1500
60		TTTTTTAAGG					1560
		ATGATTGGAG					1620
		AATGCATATA					1680
		TAGCTTTTGT					1740
		TAGGTTTCTT					1800
65		GTATCACATT					1860
		AGATATTGAC					1920
		GCAGTCATCA	TTTCACATTA	AAATGTACCA	CAGCTATATA	TOCCGCAAAA	1980
	AAAAAAAAA	AAAA					

70 Seq ID NO: 34 DNA sequence Nucleic Acid Accession #: CAT cluster

	1	11	21	31	41	51	
ac	1	1	1	1	1	1	
75	CTACTACTAA	ATTCGCGGCC	GCGTCGACTT	TTTTTTTTTT	TTGTCTTATG	TCTCTAATCT	60
		GCTCTTTTAG					120
		GGGTGTTGAC					180
		TGAAATAGCT					240
	AATTCTAAAT	TTATCTTCAC	ATACACCCTA	ACTGAGAAAA	GGGCCACATT	TTCTGCACTC	300
80	TATTAAGTAA	AGCAAATGCT	GAACTAAATG	CCTCCATGTT	AACATTTATA	TIGTTAAGTT	360
	ACTGACAGCA	TATTCTATGA	ATGATTACGT	TAGTCGTTTC	TTTAAAAAATT	ATAGGTTTGA	420
						CTAACTTCTA	480
	ACTATATATA	TACACACACA	CATGCACACA	GAATTGCCTT	CCCGGATGTA	TAGAAATTAT	540

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ATACAGCCAT GTCCAGGCCC GATGGAAATT ATGGGGGAAT ATCCAANTTA GGATACHCGT GCCGAATGGC CGGGTNTAAA TAATACHGGT TTATAATGGA CNATCCACAA TCCTGGTTTA

51

5 Seq ID NO: 35 DNA sequence Nucleic Acid Accession #: NM_018490.1 Coding sequence: 445..3300

WO 02/098358

	+	11	21	31	41	2T	
10	1	1	1			1	
10	CCGCGGCTGG	GAGACAGCGA	GCCAGAGTCT	GGGTGTTTGT	GCGAGAGCCA	CGGCGGGGGC	60
					ACCTTGAAGA		120
	TGAGAGGCCA	GGGACAGGGA	GACCGGTGCG	ATGGCAGAGC	GCGGCCCCCC	CCGCTGCGCC	180
					TGCCTCTGCG		240
	CONCOCCON.	COCCOCATAC	acceptance and a	coamagamag	GCCGCTGCGG	ccc i cmacma	300
15					CGCTCCAGCC		360
1.5							
					GAGCAGCGCC		420
	CCGGCGCGGG	AGGCGGCCGC	AGCAATGCCG	GGCCCGCTAG	GGCTGCTCTG	CTTCCTCGCC	480
	CTGGGGGCTGC	TCGGCTCGGC	CGGGCCCAGC	GGCGCGGCGC	CCCCTCTCTG	CGCGGCGCCC	540
	TGCAGCTGCG	ACCIGCICACCC	TORGGTGGAC	TGCTCCGGGA	AGGGGCTGAC	GGCCGTGCCC	600
20	GAGGGGGGTCA	GOGCOTTCAC	CCARGOGCTG	GATATCAGTA	TGAACAACAT	TACTCAGTTG	660
	COLOGGETON	COURTEDIONS	COMMOCRETA	CTACABCACC	TACRATTGGC AACTCAAAGT	OCCUPACION O	720
	CCHONHONIO	moor coors	CITICCITI	COCCERCIANO	AA COMMAN A COM	moma a coord	780
	CITICITITA	TOUNCOCKANA	OCCLIDICI	0001100000	MICICARROI	TCTANCGCTC	840
	CAGAATAATC	AGTTGAAAAC	AGTACCCAGT	GAAGCCATTC	GAGGGCTGAG	TGCTTTGCAG	
25	TCTTTGCGTT	TAGATGCCAA	CCATATTACC	TCAGTCCCCG	AGGACAGTIT	TGAAGGACTT	900
25	GTTCAGTTAC	GGCATCTGTG	GCTGGATGAC	AACAGCTTGA	CGGAGGTGCC	TGTGCACCCC	960
	CTCAGCAATC	TGCCCACCCT	ACAGGCGCTG	ACCCTGGCTC	TCAACAAGAT	CTCAAGCATC	1020
	CCTGACTTTG	CATTTACCAA	CCTTTCAAGC	CTGGTAGTTC	TGCATCTTCA	TAACAATAAA	1080
	ATTACACCC	TOROTCARCA	CTRTTTTTAT	GGACTAGATA	ACCTCCAGAC	CTTAGACTTG	1140
					CCCGTCCTAG		1200
30	MATTERIOR	ACTIOGOOGA	ALTICCIONO	OCIAI INDUIO	GAGCATTIGA	magne a magn	1260
50	CIAGGAITIC	MINGINATIC	IMITICIGIT	MICCCIGNIG	GAGCATITOA	IGGIAGGICCA	
	CTCTTAAGAA	CTATACATTT	GTATGATAAT	CCTCTGTCTT	TTGTGGGGAA	CICAGCATCT	1320
	CACAATTTAT	CTGATCTTCA	TTCCCTAGTC	ATTCGTGGTG	CAAGCATGGT	GCAGCAGTTC	1380
	CCCAATCTTA	CAGGAACTGT	CCACCTGGAA	AGTCTGACTT	TGACAGGTAC	AAAGATAAGC	1440
	AG CATACCTA	ATAATTTGTG	TCAAGAACAA	AAGATGCTTA	GGACTTTGGA	CTTGTCTTAC	1500
35	AATAATATAA	GAGACCTTCC	AAGTTTTAAT	GGTTGCCATG	CTCTGGAAGA	AATTTCTTTA	1560
						ATCTCTAAGG	1620
	APPCTAGATC	TOROTAGER	COTCATACAT	GARATTCACA	GTACAGCTTT	TGCCACACTT	1680
							1740
							1800
40							
40						GTGCTGTGCA	
						CCAGGACCAC	
							1980
	GAAGAACATA	GTCAAATAAT	TATCCATTGT	ACACCTTCAA	CAGGTGCTTT	TARGCCCTGT	2040
					GGTTCATTTT		2100
45	STEP STATE OF THE	POCONTOCIO	TO THE TOTAL OF	A CAMPTOCAT	CTTGTA CATC	a CTG corroca	2160
70	DOG: NAMEON	MCCIGCIIOI	THITTIMOO	MONTH TOWN	MCJ MCGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGGG	CTATACTOGC	2220
	TCCAMATIGE	TIMINGGCII	DOTTELLIGIE	COMMITTAL	CMIGOGRAT	CIMINCIOSC	2280
	ATCCTANCTT	TTCTTGATGC	TOTGTCCTGG	GGCAGATTCG	CTGAATTTGG	CATTTGGTGG	2280
	GAAACTGGCA	GTGGCTGCAA	AGTAGCTGGG	TTTCTTGCAG	TTTTCTCCTC	AGAAAGTGCC	2340
50	ATATTTTTAT	TAATGCTAGC	AACTGTCGAA	AGAAGCTTAT	CTGCAAAAGA	TATAATGAAA	2400
50	AATGGGAAGA	GCAATCATCT	CAAACAGTTC	CGGGTTGCTG	CCCITTCGGC	TTTCCTAGGT	2460
	GCTACAGTAG	CAGGCTGTTT	TCCCCCTTTTC	CATAGAGGGG	AATATTCTGC	ATCACCCCTT	2520
	TOTATOON	THYCOTACAGG	TODALLOCOCA	TCATTAGGAT	TCACTGTAAC	GTTAGTGCTA	2580
	men an encare	PACCAMOTOR	ATTRACTOR	COTTA TOTA CA	CTARCCTATA	CTGCAACTTG	
	IIAAACICAC	- AUGUST TTTT	ATTANTOGCC	OTTAL CIACA	CIANGCINIA	CICCONCITO	2700
55	GAAAAAGAGG	ACCITCTCAGA	AAACTCACAA	TCTAGCATGA	TTAAGCATGT		
22						ACCATTGATC	
	ACTGCAATCT	CTATCAGCCC	CGAAATAATG	AAGTCTGTTA	CTCTGATATT	TTTTCCATTG	2820
	CCTGCTTGCC	TGAATCCAGT	CCTGTATGTT	TTCTTCAACC	CAAAGTTTAA	AGAAGACTGG	2880
	AAGTTACTGA	AGCGACGTGT	TACCAAGAAA	AGTGGATCAG	TTTCAGTTTC	CATCAGTAGC	2940
	CAAGGTGGTT	GTCTGGAACA	GGATTTCTAC	TACGACTGTG	GCATGTACTC	ACATTTGCAG	3000
60	GGC3 a CCTG3	CTOTTTTCCCA	CTGCTGCGAA	TOTOTOTOTO	TAACAAAGCC	AGTATCATGC	3060
-	ANACACTECA	TRALATORON	CAGCTCTCCT	GCATTOOCNG	TOGGTTCTTC	CCLANGACCT	3120
	AMACACTION OF	COROCOS CONC.	EGGGT CT CTC	BOOK GOOK OF	TGGCTTCTTG CTGATTATGC	ACAMONAGAA	3180
	UNGGGCIACI	DOTECTORETO	TOUCACACAG	CENT OF COLUMN	CIGNITATOC	WONT CHANGING	3040
	GATTCCTTTG	TCTCAGACAG	TTCTGACCAG	GTGCMGGCCT	GTUGACGAGC	CTGCTTCTAC	3240
15	CAGAGTAGAG	GATTCCCTTT	GGTGCGCTAT	GCTTACAATC	TACCANGAGT	TAAAGACTGA	3300
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	TATTCTCATC	TTTCATCTGG	GAAGCACTTC	TGTAATCACT	GCCTGGTGTC	ACTTAGAAGA	3420
	AGGAGAGGTG	GCAGTTTATT	TCTCARACCA	GTCATTTTCA	AAGAACAGGT	GCCTAAATTA	3480
	TARATTCCTC	AGTOTAGEE	TOTOTARGOA	ATGTATGATC	TGTTTGAAAC	ASTATATAAA	3540
	CTTTGDDDDDGG	ASCETTA GOTO	TROPRORCACCA	ATATABITET	ACTIVITIES	GATCCATAAG	
70	CIIOAAAAA	ALC: INCOIO	THO I MONOCH	***********	1011111101	TTAATATTT	3660
, 0	MAGCHARTTT	MINCCIATIT	GIGIATTAAG	CACAMBATAA	AAAATATCTT	COMPARTITE	3720
	TTAAAAATCT	ATTTTAAAAAT	GTGATTTTCT	ATAACTGAAG	AAAATATCTT	GCTAATTTTA	
	CCTAATGTTT	CATCCTTAAT	CTCAGGACAA	CTTACTGCAG	GGCCAAAAAA	UUSACTGTCC	3780
5	CAGCTAGAAC	TGTGAGAGTA	TACATAGGCA	TTACTTTATT	ATGTTTTCAC	TIGCCATCCT	3840
	TGACATAAGA	GAACTATAAA	TTTTGTTTAA	GCAATTTATA	AATCTAAAAC	CTGAAGATGT	3900
75	TTTTAAAACA	ATATTAACAG	CTGTTAGGTT	AAAAAAAATAG	CTGGACATTT	GTTTTCAGTC	3960
	ATTATACATT	CCTTTGGTCC	AATCAGTAAT	TTTTTCTTaa	GEGETTTGTG	ATTACACTAC	4020
	macanasaan	GTRANAGGGT	ADDESCRIPTION OF THE PARTY OF T	TOOCTTTACT	CGATTTGGCT	ABACTACTAA	4080
	CONT. T. POCOCCO	COMMEN AREA	mamora according	**************************************	TTCATGTAAT	CONTROL OF THE LAND	4140
	CIMAIGIGGG	COLLINATING	THE CTOMOSO	WY1100100C	A TONAUGANA	GGATGTCACC	4200
80	ATGAATACIT	CUINATATEG	TIGGCTCTAC	TANTATTTC	CAMTITGCTG	GONIGICACC	
80						TTAATTAGAC	4260
	GANACGGGGA	GTAATTATGA	CACGAAGTAC	TTATGTTTAT	TTCTTAGTGA	GCTGGATTAT	4320
	CTTGAACCTG	TGCTATTAAA	TGGAAATTTC	CATACATCTT	CCCCATACTA	TTTTTTATAA	4380
	AAGAGCCTAT	TCAATAGCTC	AGAGGTTGAA	CTCTGGTTAA	ACAMGATAAT	ATGTTATTAA	4440

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TACTGGGTAT ACCATATGTA TTAG

Seq ID NO: 38 Protein sequence
Protein Accession #: AAD51172.1

75

80 | 1 1 21 31 41 51

MLRANVILLI IRTMLAEUNY PSPIPKPHPE FSSAVPEVVL NLFNCINCAN EAVVOKILOR 60

VLSKYDVERE PINGGAPPPY RISTUTYSIE OISBERGRYT ITWEFIGOVAK DSKLAYFETT 120

LINITUSHE EKLAVPEYE MISKORPPH VYERGEVOOL PEPGTYKETE KUTTAASCL 168

80

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5	YFYTGSYIRL LILTTIDSHL RRPRRVIARY LATSESLSPL VEAHGHGVTH IKBOFKCDTN	ILKFQVQREV RDKLPNISCI RYQQVVVGNV TSLSSQAPLA DHEDSNESLS	QDGLINVEDG TGESLSDLPS SDERHGHGPS MAHGQEKDSS	TVLTTITSWI LFFVFLSLLE VSSLPITPAQ TSEQARHSYG GKPNLHHGEK	SFWMNYDSSA YVYINYLFYS APLASPESLG VRFNGFQADD GVQEAGWDLD	ARVTIGLTSM RGPRRQPRRH SLTSTSEQAQ SIFPTEIRNR	240 300 360 420 480 540 600
10	Nucleic Ac:	39 DNA sequid Accession dence: 13	#: U47334.	1			
15	CGATGTCCGC	CTGAGACCGA	21 CTGTGGTTCA ATTTTGGANN CCCATGGCCA	NATGCTTGCT	ACTAACAGTA	51 TGTCAAGATA CCCGGGGCCT AGTCTGAGGA	60 120 180
20	TAGTTGCCCC TCCTGACTAC	CCAAGCCCTG GTCCCAAAGG	GCTGCTCCTT	CACTGAAGGG GTCCCGGTTC	TTCTCCTTCG	ATCTCCTTAA TGGCCTTTGG	240 300
25		40 Protein cession #: /					
	1	11	21	31	41	51	
	L	1	1	1		<u>l</u>	
30	SCPPSPGCSF	TEGFSFDLLN	DDAABKADKM			ÉKDSSSESED	60
	Nucleic Aci	41 DNA sequ ld Accession sence: 81	#: NM_0209	74			
35	1	11	21	31	41	51	
		1	CSCGCCGCCG		00000		60
			AIGGGGGTCG				120
40	CGGTGCTGCT	GCTGCTGCTG	CTGCTGCCGC	CACTGCTGCT	GCTGGCGGGG	GCCGTCCCGC	180
40	CGGGTCGGGG	CCGTGCCGCG	GGGCCGCAGG	AGGATGTAGA	TGAGTGTGCC	CAAGGGCTAG	240 300
	ATGACTGCCA	CCAAGGGGAA	CTGTGTCAGA GGCAGGCAGT	ACACACCCAC GTGBGGBCBT	CTCCTACAAG	GGBBBTGBGC	360
	теваторада	CTOTOTOCAT	CACTGTTTGA	ATATTCCAGG	CASTTATOOT	TOCACTOOTT	420
45	TTGATGGCTT	CATGTTGGCT	CATGACGGTC CATACCTGTG	ATAATTGTCT	TGATGTGGAC	GAGTGCCTGG	480
43	AGAACAATGG	CGGCTGCCAG	CATACCTGTG	TCAACGTCAT	GGGGAGCTAT	TCGGAAGAGG	540 600
	асставаета	CATGARTARG	GATCACGGCT	GTAGTCACAT	CTGCAAGGAG	accect aggs	660
	GCAGCGTCGC	CTGTGAGTGC	AGGCCTGGTT	TTGAGCTGGC	CAAGAACCAG	AGAGACTGCA ACAGCCGATG	720
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			TCGACAGGTG			GGATTCACTC	1020
55	GIGATCATTI	CTGCAAAAAC	ATCGTGGGCA	GTTTTGACTG	CGGCTGCAAG	AAAGGATTTA	1140
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	GTGACCACAG	CTGCATCAAC	CACCCTGGCA TGTGGAGACA	CATTTGCTTG	TGCTTGCAAC	CGAGGGTACA	1320
	GTCAGCAGGT	CTGTGTGAAC	ACAGTGGGGA	COTATGAATG	CCAGTGCCAC	CCTGGGTACA	1380
60	AGCTCCACTG	GAATAAAAAA	GACTGTGTGG TGCGGTAAGA	AAGTGAAGGG	GCTCCTGCCC	ACANGTGTGT	1440
	CACCCCGTGT	GTCCCTGCAC	TGCGGTAAGA	GTGGTGGAGG	AGACGGGTGC	TTCCTCAGAT	1500 1560
	AGCTARATGA	AGGCAAGTGT	TCTTCAGATG AGTTTGAAAA	ATGCTGAGCT	GTTTCCCGAG	GGTCTGCGAC	1620
65	CAGCACTACC	AGAGRAGCAC	AGCTCAGTAA	AAGAGAGCTT	CCGCTACGTA	AACCTTACAT	1680
05	GCAGCTCTGG	CAAGCAAGTC	CCAGGAGCCC CTTGAAACTA	CTGGCCGACC	AAGCACCCCT	AAGGAAATGT	1740 1800
	TGAGCTGCAT	CGTAAAGCGA	ACCGAGAAGC	GGCTCCGTAA	AGCCATCCGC	ACGCTCAGAA	1860
	AGGCCGTCCA	CAGGGAGCAG	TTTCACCTCC	AGCTCTCAGG	CATGAACCTC	GACGTGGCTA	1920
70	AAAAGCCTCC	CAGAACATCT	GAACGCCAGG TGCAGGGCTG	CAGAGTCCTG	TGGAGTGGGC	CAGGGTCATG	1980
, 0	GCATTTTATG	TCUARATGGA	ACCTTCCAAA	ATGAGGAAGG	ACAAATGACT	TGTGAACCAT	2100
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	GTGGAGGTCT	GTGTCAACCT	GGTGAATATT CCTGAAGCTG	CTGCAGATGG	CTTTGCACCT	TGCCAGCTCT	2220
75	GCCTTGCCAC	CAAACATCAG	GGAGCTACTT	CCTTTCAGGA	CIGITGAAACC	AGAGTTCAAT	2340
-	GPTCACCTGG	ACATOTOTAC	DACACCACCA	CTCACCCATATC	TATTOTTOC	CCAGTGGGAA	2400
	CATACCAGCC	TGAATTTGGA	AAAAATAATT	GTGTTTCTTG	CCCAGGAAAT	ACTACGACTG GGGGAGCTGG	2460
	GAGATTTCAC	TGGGTACATT	GAATCCCCAA	ACTACCCAGG	CAATTACCOA	GCCAACACCG	2520
80	AGTGTACGTG	GACCATCAAC	CCACCCCCCA GACTGTGGGG	AGCGCCGCAT	CCTGATCGTG	GTCCCTGAGA	2640
	TCTTCCTGCC	CATAGAGGAC	GAAACCTGCC	ACTATOTOGT	GATGCGGAAA	ACCTCTTCAT	2700 2760
			ATTCAGTTCA				2820
					10		

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5	GAGATGCAG TCAAGGCTCT AGTCCCGAGA TTTTGAGACC GGTTGGTGGG CCGTATCAGT	ATACGTGACA GCTCTATGCA GCTTGATGTC GATGTTTCCA TTACAAATGA ACAGAGCTGT GACTCATTAG	TCTGAGAACC CTGGCCCATC AGATCGTTCA CTCAGCCCAC CTTCCTTCTG AGTTCAATTT	ATCAGGAAATT CCCAGAACTA TCCGATTGCT GTGCCACTCA CATGTCAGCA TTATAGATAA	ACTTANGGAT TTTCANGTAC ACGTTCCANA ATACANATGT CAGTCOOGTA TACAGATATT	AAGAANCTTA ACAGCCCAGG GTGTCCAGGT TCTGCTATAG TTGCTGCCTC TTGGTAAATT	2880 2940 3000 3060 3120 3180 3240
10	CAGCTTCTCA TTGGTCAGCC TGTAGTGGAA CCGGCCCTCT	TTTCTTTCCC CTGCTGTGGG TAGGTGAGAC AGGAGGCCAC CTAAGGGAGC GGGAAGGAGA	CGGATGTCTT TCACCTGTCC AGAATAAGCT CCTCTGCACT	GGATAGATCA TICTGGGGTC GCTTATTCTG CGTGTGCAGG	CGGGCTGGCT TTACTCCTCC AAACTTCAGC CTCTGACCAG	GAGCTGGACT TCAAGGAGTC TTCCTCTAGC GCAGAACAGG	3360 3420 3480 3540 3600
15	ACTOMSTITE	TCCACAGCCT AGTGCTCGTG	TCTCCAGCCT	GTGTGATACA	AGTTTGATCC	CAGGAACTTG	3660 3720
20	Protein Ac	42 Protein cession #: 1	FP_066025				
25	LOONTPISYK HDGHNCLDVD DHGCSHICKE POYKWYTDGR	AAWAVLLLL CSCKPGYQGE ECLEMMGGOQ APRGSVACEC SCLEREDTVL	GRQCEDIDEC HTCVNVMGSY RPGFELAKNQ EVTRSNTTSV	GNELNGGCVH ECCCKEGFFL RDCILTCNHG VDGDKRVKRR	DCLNI PGNYR SDNQHTCIHR NGGCQHSCDD LLMRTCAVNN	CTCPDGFNLA SEEGLSCNNK TADGPECSCH GGCDRTCKDT	60 120 180 240 300
30	STGVHCSCPV SCQDVDECSL TVGSYECQCH SSDVTTIRTS PGAPGRPSTP	GFTLQLDGKT DRTCDHSCIN PGYKLHWNKK VTFKLNBGKC KEMFITVEFE DVAKKPPRTS	CKDIDBCQTR HPGTFACACN DCVEVKGLLP SLKNABLFPB LETNQKEVTA	NGGCDHFCKN RGYTLYGPTH TSVSPRVSLH GLRPALPSKH SCDLSCIVKR	IVGSFDCGCK CGDTNECSIN CGKSGGGDGC SSVKESFRYV TEKRLRKAIR	KGPKLLTDEK NGGCQQVCVN FLRCHSGIHL NLTCSSGKQV TLRKAVHREQ	360 420 480 540 600
35	TFQNEEGQMT PEAGRTSCFP KNNCVSCPGN PPPKRRILIV	CEPCPRPGNS CGGGLATKHQ TTTDFDGSTN VPEIPLPIED ARGPQVPYVT	GALKTPBANN GATSPODCET ITQCKNRRCG DCGDYLVMRK	MSECGGLCQP RVQCSPGHFY GELGDFTGYI TSSSNSVTTY	GEYSADGPAP NTTTHRCIRC BSPNYPGNYP BTCQTYERPI	CQLCALGTPQ PVGTYQPBPG ANTECTWTIN APTSRSKKLM	720 780 840 900
40	LAHPONYFKY Seq ID NO:	TAQESREMFP 43 DNA sequ 1d Accession	RSFIRLLRSK mence	VSRFLRPYK			
45	1 TTTCTTCATT	11 TTATGCTTTT ATTAATTCTC	21 CTCCCCTTTA	31 TATATACTOG	41 GOOGTITTIC TEGGGGGGCAT	51 CTTGAGAAAT	60 120
50	TTTGATATGA CTCTCCTTTC GCTTTTATAC CATTTTTTC AAACTTTAAA	CTACTACCTG TACTGGCATC CTGTGTGATG CTAAGAAACC ATACAAAGCC AAATAGGTGT	ACTGTATATA CTTTTCCATT CTCCTTGCCA TGAAAAGAAG CAGTGAAATC	GTTTCCCTTT TTACTCAATT GATATCTAGC CATGGCAAAT TACTTGGAAG	TTTTTTTTC TTCCTCAGTT AAATGCCCCC AACAGAGCTT CCAATGCTTA	CTCCCAGATT AGGITGACTT AGGATCCAAT GGAAAATAGG GAGGCAAGAG	180 240 300 360 420 480
55	TCACTTTCCA TTAAAATTGT AAATAAAGCT TTAAGGGGAT	ACATTOGAAA ATAAAAGAGA GGTTTTGGAA TTATAACAGA	GTTATGCATA AGAAATTTAA GAGCAGTGGC AGTACTTGAA	TTCCAATTGA GATATTGAAA CACTGTGATT CAGAATTGTG	GCTAGCCCTT ACTGGTAGAT GACAATGGGG AAGAGAATAG	TTARACAGCC AATAAAACCT GCACTTACTG AATTGTGCAT	540 600 660 720
60	TCTTTTATCT TCTGGCTGCA TTGAGAAAAT ATGCCTT	GCCCAGAACC ACAAAAGCAG CATAGCATNC	ACAGCTCCCA TCAAATTAAA TCCCTTTGGC	TGGGAAATAC ACATAACCCA TATAACINTT	TCCACCTCAT AAGGGGGTAC TCCACATGAA	TCTACAACCT CTAACCCAAC ATACATTCAA	780 840 900
65	Nucleic Ac:	44 DNA sequid Accession	ience 1 #: CAT clu		41	51	
70	ATGAAGTACC GACAGGGCAG GAGTAATTCA	11 TTTTTTTOGA CACTAAAGT GTGATGCTCT TAAACAACAG AGAATATTTG	TTTTAGTATG CACTGCTGTT CTTAGTCTCT AGATTATTGT	ACTATACCTT TTAGGCTACT TCACAGATCT	TTTTCCCTTT CAGTAATGAG ATTACAAAAT GGAGGCTGGA	ATTCTGATGC GTGATGAGGT ACTTCAGACT AAGTACAAGA	60 120 180 240 300
75	TATAGCGACA TGGAGTGTTC GAATCCTATG	GCAGCAGTCT TAGAATCCTA TGAGGGACAA ATTCAGAACC	TCAGGAATCC TGTGAGGGAC ACTTTCAAAC	TATGTGAGGG AAACATTCAG CCTTGTAGGA	ACARACACTO ACCCCAGCAG GTGTTCTGGA	AGAAGCCAGC TAGTGTTGTG ATCCTATGTG	360 420 480
80	Nucleic Ac:	45 DNA sequid Accession uence: 31	n #: Bos sec	quence			
	1 	11 	21 	31 	41 	51	

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GCCAAGCACG AACGGTTCCG CGCGCCTTCC TCAGAGCCTG CGCACCCTGT TCGACATCCT GACGACCIGC GCCGCGCTG CGTGCACCTC CCCACCTCCT TCTTGAAGCG CCGACGGCGG GCCCCCCGGG ACCCCACGCG CGCCCCGGGCC CGGCCCGGGG ATCAGCCGCC GCCGCCGCCG CARGOGCCTT GOTGTTCGCT CCGGCCGACG AGCCGCGGAC GGTCCTGGAG AGGAAGCCCC 240 TRACECCURAGE COMMENCE CONTROLLED GROUPS CONTROLLED ACCORDANCE 300 AGCTGTGCGC CCCGGCTGAG GCGGCGCCCT GCCCGGCGGA GCCCGAGCGG TCCCAGAGCG 360 COGCUCTGGA ACCGAGCTCC AGCGCOGACG CAGGGACGGG ACCGGGGAGC GGCTCTTCGT 420 GGACTCCGGA TCCTGGAGGG CGCCTCGGCG GGTCTGGAGG GAAAGGGCTT CATGCTTGTC GOGGTGCAGT GGCGTGCAGG GOCCTGGAGC GGACTCAGGG GATGCCCGGC GGGCTCCCCG 540 10 TGCCGGAGGG GAACGTCGGA GGCACACCAT CSCCAGCGGC GTGGACTGCG GCCTGCTGAA GACATCGGAC AGCAGCAGC GCAGGGCGCC AGCAGCAA AGCAGCAGCT GCAACGAGCT CAACGAGCT CAACGACCACC AACCCCCCCCC 600 660 GOGCCAGAGC AGAGCCAGOG COGACTITIOG GOCTGCAGGG AGCCCCCGCC CACTGGGGCG 780 GCTACTGCCC ANGGTACAAG AGGTGGCCCC GTGCCTGGGG GAGCTGCTGG CTGCAGCCTG 940 15 TRACTIONAL PROPERTY OF TRACTIONS PROPERTY PROPERTY TRACTIONAL ann CTCACCCCC GTCTGGCAGC AGCAGACCAT CCTCATGCTG AAGGAGCAGA ACCGACTCCT 960 CACCCAGGAG GTGACCGAGA AGAGTGAGCG CATCACGCAG CTGGAGCAGG AGAAGTCGGC 1020 GCTCATTAAG CAGCTGTTTG AGGCCCCCCC CCTGAGCCAG CAGGACGGGG GACCTCTGGA 1080 TTCCACCTTC ATCTAGTCCT TGTGGGCCGC GTGGGCCCCC AGGGCCAGCC TGCCACTCAG 1140 CCCTTCGAGG GTGGGGGCCC CATCGCACCC ACCCTCTCTG GCTGGAGACC CCCGGCAGGC 1200 CONTROL OF A CANADA CONTROL CONTROL DO CONTROL 1260 CTGCCCCCGG CTGGTCCCCC CACCGACGC TTGACTCCGT TTTGGCTCCT GGTTGYTGAC 1320 ATGGGCTGGG GGCTCTCTTG AGTCCGCATA GTCCGCRGCT ACTACTGGCC GCTGTCAGTG 1380 GACAGTGGGG TACCCCTCCA TGAGTTAGCG TCCCCCCGTT TCCAGCGGTG CCGCCCTGGG 1440 25 TOCCATOTTO AGGGARAGGO ACTGCCCAGG CCAGGCTGCA CTTCCAACAA COOGCAGCAG 1500 AGGGOGGGG GOOGGTCCGA CGCGGGTCCA AGGGCAGCTT CCCGCTCAAC CAGGGCACCA 1560 GOACGAGGTG COTGTAGCTC GGACGGACGG AAGTAGATGG AGGGGGTYGGG GACGGCCTGT 1620 AAGCOGGGGG TGCCTGCCTG CCTGGGGAGC CCCAGGGATA GCGGTCGGAC TTCAGGTTCT 1680 GGCCAAGGCT GAGGGACCCT GGCTGCAGCG GATCGGCACG CCGGGTGGGC GAGAGCTTGG 1740 OSCCHARGET GRODACCCT GETTEGROO GROSSERIC COGSETSSE GRAVETTES CETEGROTOS COTTOCROR A SCCHOGGST GROSSERIC COCTICTICS COGGRAGIST GCCCCACOTT GRATCCCACA CARACTECTS TRAGCCTOSC TOCCICIORG GCCCCCAGA CAGCTCCCA GCROSTATA OGRARACCT GTTCCCCC ACTROGATT TCCAAGGCCT GGGGTCCTC TCACCCCCT TFCCTCAC GCCCAGCCT TCCCCAGGST TCAGGCTGGA 30 1000 1860 1920 GAGGCCACCT CCCTCAGCCA AGGANAACGA GAACCCCCAG GGTACAGGAG GAGGCTGGGG 2040 35 CAGGTCCCCT TOGGTGTCAC TCCCTCAGCC CCTGCCCAGG CCCACTCCCG CTGGTGCTGG 2100 ACTACACAC CONSCIONA CONTROL CONTROL CONTROL ACCIDIONAL TRANSPORTA 2160 ACCAGGGCA COCCAACAGC ATGGATGGGT TCTGCAGCCC AGGGCCCCCG ATGCGGGGTC 2220 AGTGTGTGTG GGGCGCAGGG CCTCCGATGC GGGGTCAGTG CGTGGGGGGC GCAGGGCCCC 2280 CONTOCOGO TONOTO GOOGGOCGOAG GOCCODOTOS TOTOCAGGOC ACTITOGRAC 40 ACTOTOCCAC ARGGERCOTG TOTCAGAGGA GGGGCCCTGG CAGGCAGCGT GGCAACTCCT 2400 TECOGRAGOCO AGCTECATGO TARCOTGOCO ACAGCARCOC CACAGRIGOCA CATTOCCTGO 2460 TGCACCTGGT CTGCAGGGTG TCCCAGGACA GGCCCAAGTC AGCCCAGCAT GCAGCTGCCC 2520 TOCTACCOTG AAGATGGGAG TOGGCTTTCC AGGGGACATA AGGATGTCAG GCCTGGACCT 2580 CCTGGGCAGG AAAGGGTGCA GGTCCTGAGG GCCTGTGCCC CACAGCCCCA GCACCCAGGT 2640 45 GGACTGCAGC GCAGTGGGTG GGCCAGTGGC AGCCAGGGAG AAGCCCCCGG TCAGCAGGCT GGGGTCTGCC CACCAGGGCC TCCCCACGTC TCCCTTTGAG GGTGCCTGCC ATGCCCTGGG 2700 2760 GGATCCTGGC ATCTTTACTG GACTGGAAGC AGGAGACAGA ACAGTGTCTG TCCCGGGGTG 2820 ACTICATCAG GAGACCGCCC ACATAGAGCI GGACCCCGCA GCIGAAGCGG AAAIGIGAGA CAGGCTGGCA CCTCCGGAAA AACTGCCTTT CAGCCTTGGT GTTCCGTGCA AGGTGAAAAG 2940 50 ANATAGGTCC TOCCAGTTA CAGCITGANA TCAGGCTAGT GAGTGGCCCT GGAGACCACG 3000 AGGGRADA TO THE ANGGOOD COGCTOGCEG GOTOPEGGTG GOTOGCEGEG GOTOPEGGEG 3060 ACCCIGCCIG GAGCCTGCCC TAGGACGCTG GGCGGGTCAG TCTCCGTGCA GGATGTGAGC 3120 AGCGTCCCTG GGCTCTATCC GCGAGGTGCC AGTAGCGTGT GCAGGTACAT ACACGTGCGT 3180 GCACACTGTG ATGACACCCG GAAATGTCTC AGGATGTTGA AATGTGTCCT TGGGGGCAGA AGTGTCCCCA GTTGAGAATC TGCCCCAGAG GAACACACCC ACACCAGGCC TCAGGATTTT 3300 GTGTTGATCA ACTTCCAAGG RAAAGGAACA TCTCAGCCGG GCGTGGTGGT TCACGCCTGG 3360 ANTOCCAGOA CHIMAGGOCA GGAGTTCCAG AGCAGCCTGG GCAACGCAGT GAGAGACCCC 3420 ATCTCTACAA DARRAADAAA AGAAAGAAAG ARAATGAGAG ATCCAGGTTT AAAAATTCAT 3480 ANACACCACA AGGAAACAAT ACACTATGAG ACCCAGCAGA AGCAACAGAT TGACTCTAGA 3540 60 CCCAGATACT AGAATTATCA GAGAGAATAT AAAGTAACAG TGTTTTATAT ATCTAAAGAA 3600 ATAAAAGAGA TITCIGGAAA CATGAAAAAA AA Seq ID NO: 46 Protein sequence Protein Accession #: Bos sequence 65 21 31. 41 51 NKVESRGPPS CHLRARASHS CLMSADFSCS SCVMRSLFSV TSWVRSRPCS FSMRMVCCCQ TGGEVDVRAG OGGPEEDGGR ARLAOAAASS SPRHRATSCT LGSSRPSCRG LPAAPKSALA 120 70 LLWPRRRWRS CIRCSCCWYO SRPRAIISKP CSSTSFSCSS SPICPSRPOS TPLANVCLRR 180 SPRANGARRA SPESAPGPCT PLHROKHEAL SLQTREGALQ DPESTKSRSP VPSLRPRWSS 240 VPAPRSGTAR APRGRAPPOP GRTAAPGOGR REWDRPEGRA RPCAGASSPG PSAARRPERT 300 PRRIRRRRL IPGPGRGARG VPGGPPSALQ EGGAQVHAAA PPVVRMSNRV RRL

75 Seq ID NO: 47 DNA sequence Nucleic Acid Accession #: NM_020957.1 Coding sequence: 1156..3486

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	ATGAMATGT	TCTAAAATTG	TGATGGCGGA	TGCACACCTC	TGAATATATT	AAAAGCCATT GAGATTTGCT	360 420
5	TYCPPPPYCOCA A	TICEATTTTCC	AATAACTTGA	AAGTTGTAAA	AACTCACACT	TCTCAGGGTT	480
-	AGGTCTCAGA	AAGAAAAGGA	AGTAATTTAT	TCTTTAATAA	AGCAATTGTT	AAATACTCTT TAGGTACCAT	540
	TAGAACTACC	ACTGATTGCA	ATTTTGCAGT	GTCTACTCAT	AGTGTCTATA	TAGGTACCAT	600
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1.5	CAGCTCCAGG	ATCCAGCAAA	COGTTTTCCCA	AAGCCTGGAA	GCAAAAGAAT	AGCTGAGCCA	1020
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20	AATGATAACG	CTCCTGAGTT	TGAGCAGCCC	ATCTACAAAG	TGCAGATTCC	AGAGAACAGT	1920
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	AAAATATCAT	ACACACTCTT	TCAGCCTTCG	GAGGATATTA	GTAAAACTTT	GGAGGTAAAT TACGTCTTAT	2040
	0110maaaa	marks agains a	NO TOGGGGG	CONCERNION OF	CARACHOCAC	TOTTO CTO CTO	2160
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	TCAGTCAAGA	ACTTTTACAC	CTTGGTAACG	GAGAGAGCAC	TCGACAGAGA	AGCAAGAGCT	2400
	GAATATAATA	TCACCCTCAC	CGTCACAGAT	ATGGGGACTC	CANGGCTGAA	AACGGAGCAC	2460
40						CCAAACCTCC	
+0	h Cagh Caghg	ACTICAGGGA	CARCARCAGO	OTCA CCTA CT	COLLICERCE	GCCCCAGGAC CCTGTTCGCC CGCCACAGAC GGACGCCAAC	2640
	COGCACCTGC	COCTOSCOTO	CCTGGTCTCC	ATCARCGCAG	ACAACGGCCA	CCTGTTCGCC	2700
	CTCAGGTCCC	TGGACTACGA	GGCCCTGCGG	GAGTTCGAGT	TCCGCGTGAG	CGCCACAGAC	2760
	CGCGGCTCCC	COCCTTTGAG	CAGCGAGGCG	CTGGTGCGCG	TGCTGGTGCT	GGAGGCCAAC	2820
45	GACAACTCGC	CCTTCGTGCT	GTACCCGCTG	CAGAACGGCT	CCGCGCCCTG	CACTGAGCTG	2880
	GTGCCCCCGGG	CGGCCGAGCC	GGGCTACCTG	GTGACCAAGG	TOGTGGCGGT	GGACGGCGAC CGGGCTGTTC	2940
	TOGGGCCAGA	ATGCCTGGCT	GTCGTACCAG	MOCCOCAGO	TOTAL COCK	GCGCGACGCA	3000
	CCCAACCACA	COCTOCTOCT	GCTGCTCAAG	GACAATGGCG	AGOTTOTAGG	CTCGGCCACC	3120
50	GCCACGCTGC	ACGTGCTCCT	GGTGGACGGC	TTCTCCCAGC	CCTTCCTGCC	CTCGGCCACC GCTCCCAGAG	3180
	TCGCTCTCCT	CCCTCTTCCT	CTTTTCGGTG	CTCCTGTTCG	TGGCGGTGCG	GCTGTGCAGG	3300
	AGGAGCAGGG	COCCTOGGT	GGGCCGCTGC	TCGATGCCTG	AGGGCCCCTT	TCCAGGGGGT	3360
55	CTGGTGGACG	TAAGCOUCAC	COGGACCUTG	TCCCAGAGCT	ACCAATACGA	GGTGTGTCTG	3420
55	CCTTAGGGCA	CTAGGAAAGA	DATACATTAA	PARTOCACOC	TTCACAATAG	CTTTTGGATTT	3540
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	TAMACETTE	CTTALACTOR	CTTTCCCTTCCT	TOO INTILITY	OIIOGGCICA	TTTTTTCTT	4020
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	GTTGCCCAGG	CTGATCTTGA	ACTOCTGGGC	TCAAGCCATC	CTCCCTCCTC	AGCCTCCCAA	4260
70	AATTCTOGGA	TTACAGGCAT	AAGCCAATGT	GCCCATCCAA	AGTTTTATTT	ATTTATTTT	4320
70	TIGAGATGGA	GICTOGTAAA	GITACCTITA	AAAAAAAAGT	TUTATTTTCC	CTGTATTGGT	4380
	CTTATCTCCTTAA	ALMOUNTARA	GARGECATUG	TRACACATTO	ACTIVITIETA	TITAACCAGC AATGTGTTTG	4500
	TACTGAATTA	AAAAATCAGA	GGTCCCTGTT	ATATTTTTAA	TGGCTAACAA	CTCAATCTCA	4620
75	TTAAGTTGGA	AAAAAAACTT	ATCAAAGAGA	CATTTACATG	GTTTGGCTTT	TATATTCATC	4680
	ATAGTATACA	TTGGCCGTAT	CTAGCCCTTT	CTCTCTAAAA	TATCCCTATG	TTTAATCTGT	4740
				TICTITCTAG	ATATTAGGCC	TTTGAATAAA	4800
	MITCHATGTG	AGTCAGAAAA	MARAAA				

Seq ID NO: 48 Protein sequence Protein Accession #: NP_066008.1

1 11 21 31 41 51

5	TRKARIISQG LRVIDINDHS LIHEFRDGRK EFEQPIYKVQ	PMPTEKEMIL YPELVLDKEL IPENSPLGSL	TGDLLINEKL KIPENSPLGT DREEEPQLRL VATVSARDLD	DREELCGPTE EFPLNHALDL TLTALDGGSP GGANGKISYT	PCILHFQVLM DVGSNNVQNY PRSGTAQVRI LFQPSEDISK	TLEVNPMTGE	60 120 180 240 300
10	PEIVVAVPSV LTVTDMGTPR GTNAQVTYSL LSSEALVRVL WLSYOLLKAT	SDPDSGNNGK LKTERNITVQ LPPQDPHLPL VLDANDNSPF EPGLFGVWAH	TISSIQEDLP ISDVNDNAPT ASLVSINADN VLYPLQNGSA NGEVRTARLL	FLLKPSVENF FTQTSYTLFV GHLFALRSLD PCTELVPRAA SERDAAKORL	YTLVTERALD REMNSPALITI YEALREFEFR EPGYLVTKVV VVLUKDNGEP	ALTSPIPENS REARAEYNIT GSVSATDRDS VSATDRGSPA AVDGDSGQNA PRSATATLHV VRLCRRSRAA	360 420 480 540 600 660 720
15	SVGRCSNPEG Seg ID NO:	PFPGRLVDVS	CTCTLSQSYQ	YEVCLTGGSE	TSEPKPLKPI	IPNFSP	
	MODIFIC NO.		1 #1 CAL GI	ascer			
20	AATTAGAATG	GTACATGGTA	CATCTAAATG	TATGTTTATA	TATTTTATTT	51 TGTCTAAATA GTGCATTTTA TAATGTAGTA AGCTATTGTC	60 120 180
25	AACGAAATAA TACAATGTTT	AAATTGTGCA ATGCTTCACA	ATCTCTAAGC	ACATGAACTA GAGACTGCAA	TGTATTATTT	GTACAGCATG CTGGGACAAA	240 300 360 420
30	Nucleic Ac:	50 DNA sequid Accession	a #: AP0347	99.1			
0.5	1	11	21	31	41	51 .	
35		00000000000	0.0.0.0.0.0.0	000000000000000000000000000000000000000	1	TGCCAGCAGG	60
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	AGAAAATGAG	TENGCARATA	AAGAAGCTAT	CCTACGGCAG	ATGGAAGAGA	AAAACAGACA	1320
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	CTTGGTAGAT	GCAAGAATGT	TAGATCACCT	AACAAAAAA	GATCTCCGTG	TCCATTTAAA	3360
	AATGGTGGAT	AGTTTCCATC	GAACAAGTTT	ACAATATGGA	ATTATGTGCT	TANAGAGGTT	3420
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	CGTGTTGGTG	TGGAGCAATG	ACCGAGTTAT	TCGCTGGATA	CANGCAATTG	GACTTCGAGA	354
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	CTTTGACTAC	AGCAGCTTAG	CTTTATTATT	ACAGATTCCA	ACACAGAACA	CCCAGGCAAG	366
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15	TGAAAGTGAT	CACAAGAACT	TCAGACGTGG	ATCAACCTOG	AGAAGGCAGT	TTCCTCCTCG	378
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	GCAGCACTGA	CCTCCTATGG	CCTCTTTTCA	GTCTACTCTA	CCTAAAGTGC	ACTACCATOR	402
20	AAGAAGACGA	GCAGTGAAAA	CCTTTGTGAA	AACTGAATTC			

Seq ID NO: 51 Protein sequence Protein Accession #: AAC26100.1

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25	1	11	21	31	41	51	
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		EDTPMSQRGS					60
	QRLQDVIYDR	DSLQRQLNSA	LPQDIESLTG	GLAGSKGADP	PEFAALTKEL	NACREQLLEK	120
						VEVLKALKSL	180
30						ASSEGSTESE	240
		VHEKRLSNGS					300
						QRESTSINDM	360
		KEAILROMEE					420
25						RLLTESNERL	480
35		PERMATI I DE					540
		TSABLRYSVG					600
		SHPFESDTEM					660
		KESTELRABE					720
40		SPAREMDRMG					780
40						KSSIGRLFGK	840
						KGLPFAQWDG	900
						RLKLRLAIQB	960
		PTSRTPSGNV					1020
45		SLGLPQYRSY					1080
		LERRREASOH					1140
		ALLLQIPTQN					1200
	FPPREVHCIS	MMPGSSETLP	AGFRLTTTSG	QSRKMTTDVA	SSRLQRLDNS	TVRTYSC	

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WO 02/098358 PCT/US02/17594

It is understood that the examples described above in no way serve to limit the true scope of this invention, but rather are presented for illustrative purposes. All publications, sequences of accession numbers, and patent applications cited in this specification are herein incorporated by reference as if each individual publication or patent application were specifically and individually indicated to be incorporated by reference.

WHAT IS CLAIMED IS:

 A method of detecting an androgen-independent prostate cancer cell in a sample from a patient having undergone androgen ablation therapy, the method comprising determining the presence or absence of a nucleic acid comprising a sequence at least 80% identical to a sequence as shown in Tables iA-4.

5

- The method of claim 1, wherein said determining is by hybridizing with a
 polynucleotide that selectively hybridizes to a sequence at least 95% identical to a sequence
 as shown in Tables 1A-4.
- 10 3. The method of claim 1, wherein the biological sample:
 - a) is a tissue sample; or
 - b) comprises isolated nucleic acids.
 - The method of claim 3:

immobilized on a solid surface.

- 15 a) wherein the nucleic acids are mRNA; or
 - b) further comprising the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide.
 - The method of claim 2, wherein the polynucleotide:
 - a) comprises a sequence as shown in Tables 1A-4;
 - b) is labeled, including a fluorescent label; or
 - c) is immobilized on a solid surface.

identical to a first sequence as shown in Tables 1A-4.

- The method according to claim 1, wherein said biological sample is contacted with a
 plurality of polynucleotides that each selectively hybridizes to a sequence at least 95%
- 7. The method according to claim 6, wherein said plurality of polynucleotides are

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 An isolated polypeptide which is encoded by a nucleic acid molecule having polynucleotide sequence as shown in Tables 1A-4.

An antibody that specifically binds a polypeptide of claim 8.

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- 10. The antibody of claim 9:
 - a) further conjugated to an effector component, including a fluorescent label a radioisotope or a cytotoxic chemical; or
 - b) which is an antibody fragment or humanized antibody.

- 11. A method of detecting an androgen-independent prostate cancer cell in a patient having undergone androgen ablation therapy, the method comprising contacting a samp from said patient with an antibody of claim 9.
- 45 12. The method of claim11, wherein:
 - a) the antibody is further conjugated to an effector component, e.g., a fluorescentabel; or.
 - b) said sample comprises a cell.
- 50 13. A method of detecting antibodies specific to androgen-independent prostate can a patient having undergone androgen ablation, the method comprising contacting a biolisample from the patient with a polypeptide encoded by a nucleic acid comprising a sequence from Tables IA-4.
- 55 14. A method of inhibiting proliferation of androgen-independent prostate cancer ce a patient having undergone androgen ablation therapy, the method comprising administ to the patient a therapeutically effective amount of a compound that specifically elimina cells expressing an antigen listed in Tables 1A-4.
- 60 15. The method of claim 14, wherein the compound is an antibody.
 - A drug screening assay comprising the steps of:

 a) administering a test compound to a mammal having a prostate proliferative condition or a cell isolated therefrom:

- b) comparing the level of gene expression of a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4 in a treated cell or mammal with the level of gene expression of the polynucleotide in a control cell or mammal, wherein a test compound that modulates the level of expression of the polynucleotide is a candidate for the treatment of prostate cancer.
- 17. The assay of claim 16, wherein:

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- a) the control is a mammal with prostate cancer or a cell therefrom that has not been treated with the test compound; or
- 75 b) the control is a normal cell or mammal.
 - 18. A method for treating a mammal having a prostate proliferative condition or prostate cancer comprising administering a compound identified by the assay of claim 16.
- 80 19. A pharmaceutical composition for treating a mammal having a prostate proliferative condition or prostate cancer, the composition comprising a compound identified by the assay of claim 16 and a physiologically acceptable excipient.
- 20. A method of detecting a prostate cancer associated transcript, the method comprising contacting a biological sample from the patient with a plurality of polynucleotides wherein at least two of said polynucleotides selectively hybridize to a difference sequence at least 80% identical to a sequence as shown in Tables 1A-4.
 - 21. A method of detecting a prostate cancer, the method comprising the steps of:
 - a) providing a biological sample from a patient;
 - b) contacting the biological sample with a first polynucleotide that selectively hybridizes to a sequence at least 80% identical to a first sequence as shown in Tables 1A-4, to determine the level of a prostate cancer-associated transcript in the biological sample; and with a second polynucleotide that selectively

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95 hybridizes to a second sequence at least 80% identical to a sequence not shown in Tables 1A-4; wherein the expression of said second sequence is not substantially changed in prostate cancer, to determine the level of expression of a control transcript in the biological sample; and

- c) comparing the level of the prostate cancer-associated transcript to a level of the normal tissue associated transcript in the biological sample.
- 22. A method for quantitation of a prostate cancer-associated transcript in a cell from a patient, the method comprising contacting a biological sample from the patient with a polynucleotide that selectively hybridizes to a sequence at least 80% identical to a sequence as shown in Tables 1A-4.
- 23. The method of claim 22, wherein:
 - a) the polynucleotide selectively hybridizes to a sequence at least 95% identical to a sequence as shown in Tables 1A-4;
- b) the biological sample is a tissue sample;
 - c) the biological sample comprises isolated nucleic acids;
 - d) the nucleic acids are mRNA;
 - e) further comprising the step of amplifying nucleic acids before the step of contacting the biological sample with the polynucleotide;
 - f) the polynucleotide comprises a sequence as shown in Tables 1A-4;
 - g) the polynucleotide is labeled, including a fluorescent label; or
 - h) the polynucleotide is immobilized on a solid surface.
 - A biochip comprising a plurality of polynucleotides that selectively hybridize to a sequence at least 80% identical to a sequence as shown in Tables 1A-4.
 - 25. A method of screening drug candidates comprising:
 - a) providing a cell that expresses an expression profile gene selected from the group consisting of an expression profile gene set forth in Tables 1A-4 or fragment thereof;
 - b) adding a drug candidate to said cell; and

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 determining the effect of said drug candidate on the expression of said expression profile gene. Page 210 of 210

130 26. A method according to claim 22 wherein said determining comprises comparing the level of expression in the absence of said drug candidate to the level of expression in the presence of said drug candidate.